

A Guide to Immunization for Canadians

Second Edition – 1984

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Endorsement: This edition of the Guide has the approval of the Boards of Directors of the Canadian Medical Association and the Canadian Paediatric Society.

Foreword

Some significant changes in immunization practice have occurred since the first edition of this Guide was published in 1980. In order that the greatest benefit may be gained from immunizing agents, information on their availability and optimum usage must be kept current. Accordingly the National Advisory Committee on Immunization has revised and expanded the Guide to take into account the licensure of new or improved vaccines and immune globulins and has modified its recommendations on the usage of certain other agents. It is hoped that the wide distribution of this Guide will contribute to the attainment in Canada of the best possible protection of the population that currently available agents allow. I also hope it will encourage adoption of uniform immunization policies and practices throughout Canada.

Among noteworthy changes in this second edition are the inclusion of recommendations on the use of the recently licensed hepatitis B vaccine and the new human diploid cell rabies vaccine, new sections on adult immunization and immunization for health care workers, relegation of mention of smallpox vaccine to a historical note now that global eradication of smallpox has been achieved, and deletion of the section on typhus vaccine which is no longer manufactured. The recommendations regarding rubella vaccine have undergone major revision, elimination of indigenous measles is addressed, and some changes have been made in the recommended schedules for immunization of infants and children.

Immunization practice is constantly changing as a consequence of both development of new immunizing agents and alterations in disease incidence, and the Committee will make new recommendations or adjust existing ones in response to such changes. New and revised recommendations are published promptly in Canada Diseases Weekly Report, a publication of Health and Welfare Canada. Readers who wish to comment on the Guide or any of the separately published recommendations are invited to write to the Secretary of the Committee.

It is again a pleasure to acknowledge the valuable advice given to the Committee by members of the national advisory committees of the United States (Immunization Practices Advisory Committee) and United Kingdom (Joint Committee on Vaccination and Immunisation). The collaboration and contributions of representatives of the Canadian Medical Association and the Canadian Paediatric Society have also been greatly appreciated.

The Committee is most grateful to Dr. Stanley Acres of the Bureau of Epidemiology for his many contributions to its activities; his efforts have greatly facilitated the appearance of both editions of this Guide.

Finally, it is again a pleasure to thank Dr. A.B. Morrison, Assistant Deputy Minister, Health Protection Branch, for his continuing support and encouragement.

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Part 1

General Considerations

Introduction

The range of immunizing agents licensed for use in Canada is continually increasing as a result of the introduction of new vaccines and immune sera; and improvements in or modifications to currently available preparations are often made. The use of these agents for both active and passive immunization must therefore be evaluated continually in relation to the prevalence and significance of the diseases against which they confer protection. When the incidence of a particular communicable disease falls, perhaps as the result of widespread use of an immunizing agent, the need for a continuation of the immunization program concerned must be reappraised and, indeed, may be questioned by the public. There is a danger that successful immunization programs might lead to future apathy regarding vaccine use and the likelihood of a resurgence of the disease unless it can be totally eradicated. While the ultimate aim of those concerned with immunization is the elimination of vaccine-preventable diseases, eradication is usually a practical possibility only in infections restricted to man and involving no other host, such as smallpox and measles.

An ideal vaccine should confer long-lasting, preferably lifelong, protection against the disease; it should be inexpensive enough for large scale use, stable enough to remain potent during shipping and storage, and have no adverse effect on the recipient. Some vaccines come close to meeting these criteria; others do not. Each vaccine has its own characteristics, and generalizations are difficult to make; consequently, each is considered separately in this document.

Some vaccines consist of inactivated microbes or of purified protective fractions derived from them. Others, particularly vaccines against viral diseases, contain live microorganisms. These have the advantages that the dose is small, because the virus replicates within the recipient and that the immunity lasts for many years. However, they

demand particular care in many ways: in storage, when they may inadvertently be inactivated; in the choice of the individual immunized, since they are not appropriate for immunodeficient persons, or in some cases during pregnancy; and with regard to changes in virulence and possible spread to contacts of vaccinees and to the environment.

In this booklet, information is presented on the immunizing agents available in Canada and their use in the prevention of communicable diseases. The recommendations by the Committee on routine immunization of infants and children are discussed in some detail, and an attempt is made to answer most of the day-to-day queries regarding immunization.

Because of variation among manufacturers' products, precise details on the dosage and route of administration of individual products are not given. Readers are referred to manufacturers' labelling and package inserts for this information.

General Cautions and Contraindications

Minor infections, such as the common cold, are very prevalent in pediatric age groups and are not contraindications to immunization; however, any febrile illness is a reason to defer immunization. This precaution is to avoid the superimposition of adverse effects from the vaccine on the underlying illness, or mistakenly identifying a manifestation of the underlying illness as a complication of vaccine use.

If a severe untoward reaction follows an injection of any vaccine, the physician should postpone further doses, report the reaction and seek expert advice. The use of fractional doses for continuation of a course of vaccine is not recommended in these circumstances.

Eczema and atopic disease in general are not contraindications to immunization unless the individual is allergic to a specific vaccine component.

Vaccines prepared in embryonated chicken eggs or in chick embryo cell cultures may cause hypersensitivity reactions in some patients. The likelihood of such reactions occurring varies considerably between vaccines. Yellow

fever vaccine and influenza vaccines are prepared from viruses grown in embryonated eggs. They should not be given to persons known to be hypersensitive to eggs. Measles and mumps vaccines are prepared in chick embryo cell cultures. A small number of hypersensitivity reactions to measles vaccine have been reported in persons who on eating eggs suffer anaphylactic hypersensitivity manifested by hives, swelling of the mouth and throat, difficulty in breathing, hypotension, and shock. Such individuals may be identified by inquiry about the occurrence of ill effects on eating eggs. Persons with anaphylactic hypersensitivity to eggs should not be given measles or mumps vaccines; however, individuals allergic to eggs but whose allergies do not include anaphylactic symptoms may be given these vaccines, as may persons allergic to chickens or feathers.

Some vaccines contain preservative (e.g. thiomersal, a mercurial) or trace amounts of antibiotics (e.g. neomycin) to which patients may be hypersensitive. No currently recommended vaccine contains penicillin or its derivatives.

Epinephrine should always be immediately available when immunizing agents are injected in order to treat the extremely rare but serious complication of anaphylaxis.

Live Vaccines

Immunizing agents which contain living micro-organisms (measles, rubella, mumps, BCG, yellow fever or oral polio vaccines) **must not be given to patients with conditions in which the immune mechanism is impaired**, including:

- a) patients with immune deficiency diseases such as hypogammaglobulinemia or combined immunodeficiency;
- b) patients with altered immune status due to diseases such as leukemia, lymphoma, or other generalized malignancy;
- c) patients with immunosuppression induced by therapy with corticosteroids, antimetabolites, alkylating drugs or radiation.

Individuals residing in the household of an immunocompromised individual should not receive oral polio vaccine because vaccine viruses are excreted by the recipient of the vaccine and may be communicable to other

persons. This precaution does not apply to other live virus vaccines.

Immunization and Pregnancy

When indications for their use are present, inactivated vaccines and toxoids may be given to pregnant women, although it is preferable to defer immunization until after delivery unless immediate risk is involved.

Live viral vaccines should not generally be given to pregnant women because of theoretical risk to the developing fetus. Rubella and measles vaccines are contraindicated in pregnancy and other means of protection should be used for susceptible pregnant women. For some other diseases, such as yellow fever and poliomyelitis, the risk of disease may outweigh any theoretical risk to the fetus and vaccine may be given if exposure is likely.

Combined measles, mumps and rubella (MMR) and oral polio vaccine (OPV) may be administered with safety to children of pregnant women. Breast feeding does not interfere with immunization and infants who are breast fed should receive all recommended immunizations at the usual times. Similarly, lactating mothers may safely be given rubella vaccine when it is indicated.

Immunization of Children with Neurologic Disorders

Considerable controversy exists concerning the administration of pertussis vaccine to children with neurologic disorders. If the condition is stable the advantages of protection against disease generally outweigh the risks. If the condition is evolving or changing, vaccination is contraindicated. Readers are referred to the section on pertussis vaccine.

Immunization During Immunosuppressive Therapy

Individuals receiving immunosuppressive therapy may respond poorly to active immunization procedures. For patients on short-term therapy, immunization should be deferred until treatment is discontinued. For those on long-term therapy, inactivated vaccines may be used but live vaccines should be deferred. The usual protective immune

response to vaccines may not occur in the immuno-suppressed patient. Accordingly an extra booster dose of any inactivated vaccine that has been used may be required after therapy is discontinued unless antibody titres are shown to be adequate.

Immunization of Hemophilic Children

Immunization should be carried out using a fine needle, followed by application of firm pressure without rubbing to the injection site for at least 5 minutes after the injection. Administration can be subcutaneous or intramuscular depending on the product. If there is concern that an injection may stimulate bleeding, it can be scheduled shortly after administration of anti-hemophilia therapy.

Immunization of Infants Born Prematurely

Prematurity is not a reason to defer immunization. Antibody response to immunization is a function of post-natal age and not of maturity. In infants born prematurely, maternal antibody is present at lower titres and for a shorter duration than in mature infants. Infants whose clinical condition is satisfactory should be immunized with full doses of vaccines according to the recommended schedule for normal infants and children. To avoid virus dissemination, administration of oral polio vaccine to a premature infant in a hospital nursery should be deferred until after discharge.

Timing of Vaccine Administration

For products that require more than one dose or booster doses for full immunization, intervals between doses that are longer than those recommended **do not** lead to a reduction in final antibody levels. Therefore, **Interruption of a recommended series of immunizations for any reason does not necessitate starting the series over again, regardless of the interval elapsed.** By contrast, doses at less than the recommended interval may result in less than optimal antibody response and should not be counted as part of a primary series.

There are obvious practical advantages to giving more than one vaccine at the same time especially in preparation

for foreign travel or where there is doubt that the patient will return for further doses of vaccine. Most of the commonly used antigens can safely be given simultaneously. Commercially prepared combinations of vaccines are convenient to use.

Inactivated vaccines can be given simultaneously, but at separate sites, bearing in mind the precautions that apply to each individual vaccine. Since reactions may be additive, vaccines such as cholera and typhoid which are commonly associated with local or systemic effects should be given on separate occasions whenever possible.

While most inactivated and live vaccines may also be given simultaneously at separate sites, the antibody response to cholera and yellow fever vaccines may be reduced if they are given simultaneously. When circumstances allow they are preferably separated by at least 3 weeks although no diminution in protection has been demonstrated when they are given simultaneously.

Live vaccines should never be mixed in the same syringe, but may be administered simultaneously at different sites. One live vaccine may interfere with the effectiveness of another, and to minimize this possibility two or more live vaccines should preferably be administered either on the same day or be separated by an interval of at least one month.

Recent Administration of Immune Globulin or Hyperimmune Globulin

Because passive immunization can interfere with the response to live virus vaccines, the administration of measles, mumps and rubella vaccines should be postponed for about three months after administration of immune globulin. When it is necessary for immune globulins to be administered within two weeks of measles, mumps and rubella vaccine, the MMR vaccination should be repeated three or more months later. Immune globulins do not generally interfere with the response to inactivated vaccines given concurrently.

Storage and Handling of Immunizing Agents

Immunizing agents are biologically active materials which are subject to gradual loss of potency from deterioration and denaturation. Such loss of potency may be accentuated by transportation or storage under less than the optimal conditions prescribed by the manufacturer. This can result in inadequate protection and a false sense of security for vaccinees. **Recommended conditions for storage outlined in the manufacturer's package insert should be carefully followed.** Storage temperatures should be regularly monitored and recorded. Adequate temperature control must also be maintained during transportation and field use.

In general, the following principles apply:

- 1) Vaccines should not be used beyond their expiry date.
- 2) Vaccines should be stored under refrigerated conditions as recommended by the manufacturer until the time of use. Storage in the door of a refrigerator should be avoided because fluctuations in temperatures are more likely there. Multi-dose containers should be returned to the refrigerator immediately after each use. Measles, mumps and rubella vaccines must be protected from light at all times to avoid inactivation.
- 3) Inactivated vaccines must be discarded if they are inadvertently frozen.
- 4) Live virus vaccines may be used after they have been frozen but repeated freezing and thawing should be avoided. Live oral poliovirus vaccine (OPV) should not be refrozen after it has been thawed; it should be refrigerated and used within 90 days of thawing. Once opened, OPV dispensers may be used for up to three days, provided they are refrigerated constantly.
- 5) Reconstitution of vaccines, if required, should be done immediately prior to use, and only with the diluent provided by the manufacturer for that purpose. If unused, reconstituted vaccines should be discarded at the end of the work day. Yellow fever vaccine should be used within one hour of reconstitution.

Immunization Technique

Immunization should be given by the route of administration recommended by the manufacturer for each vaccine. The injection site should be carefully chosen to avoid major nerves and blood vessels. The best sites for subcutaneous or intramuscular immunizations are the deltoid area or the anterolateral surface of the thigh. The latter is the site of choice for infants and young children whose deltoid muscle is very thin. The buttock is not recommended as an immunization site except when large volumes must be given, e.g. immune globulin. If it is used, care must be exercised in avoiding injury to the sciatic nerve by selecting a site in the upper outer mass of the gluteus maximus and avoiding the central area.

Children should be well restrained before any injection. The chosen site should be cleansed with a suitable antiseptic such as isopropyl alcohol, which is allowed to dry on the skin before the injection is given.

A separate, sterile needle and syringe should be used for each immunization, and should be carefully disposed of after use. An appropriate size and length of needle should be chosen to ensure that the vaccine is deposited within the proper tissue layer.

For intradermal injections, choose a fine gauge needle (e.g. 26-27 gauge). With the bevel facing upwards, insert the needle under the outer layer of skin at an angle almost parallel to the skin. Insert the needle so that only the bevel penetrates the skin. Inject the solution slowly; if done correctly a small bleb or blister should appear.

For subcutaneous injections, a 25 gauge needle is recommended. It is inserted at a 45° angle into the tissues below the dermal layer of the skin. For intramuscular injections, a longer needle is needed. After inserting the needle into the site, pull back on the plunger to determine if a blood vessel has been entered. If so, withdraw the needle and select a new site, using a new needle for each insertion.

Immunization Records

Each person who is immunized should be given a permanent personal immunization record. Individuals should

be educated to keep these record cards with them at all times (e.g. in their wallet) and to produce their card for updating whenever they receive an immunization. Parents should keep and maintain these records on behalf of their children.

The health care provider must also maintain a permanent record of the immunization history of each individual. This office record should contain the name of the vaccine, date given, dose, manufacturer and lot number.

Physicians should try to keep everyone under their care up to date on immunizations, and ensure that series are completed and boosters are given at the appropriate intervals. A child's entry to day nursery or school provides a good opportunity to review immunization status and provide whatever updating is required.

Adverse Reactions

Local or systemic adverse reactions may follow use of immunizing agents. Most are mild and self-limited. Rarely, serious or unexpected adverse reactions may occur. The majority of reactions follow shortly after vaccination but others may not be manifest for some time. Health personnel should be aware of the incidence and nature of adverse reactions to immunizing agents and should inform patients or parents of these possibilities in relation to the benefits of immunization and the risks of the disease. Parents and patients should be encouraged to report any adverse reactions.

Health personnel should report adverse reactions, especially severe or unusual reactions, to the local health department.

Local reactions usually consist of induration, tenderness and redness at the injection site. More severe reactions, e.g. edema and abscess formation, occasionally occur.

Systemic reactions may include fever, rash, joint or muscle pains, arthralgia, myalgia, fainting, seizures or other central nervous system symptoms. Most of these reactions subside within 48 hours. Fainting immediately after immunization is usually due to apprehension.

Allergic reactions such as urticaria, rhinitis, bronchospasm and anaphylaxis are rare. They may be due to specific

allergy to any component of the vaccine (which may include antibiotics, egg protein or preservatives).

Severe reactions, local or systemic, may indicate that additional doses of the same agent should be avoided. The physician should seek expert advice in such an instance.

Part 2

Recommended Immunization for Infants, Children and Adults

A. Recommended Immunization Schedules for Infants and Children

Few measures in preventive medicine are of such proven value and as easy to implement as routine immunization against infectious diseases. Immunization carried out as recommended in the following schedules will provide good basic protection for most children against the diseases shown.

With respect to tetanus and diphtheria, the schedules pertain to use of either fluid or adsorbed toxoids, but in view of their superior antigenic properties, the use of adsorbed products is recommended.

Both live and inactivated polio vaccines have been used in Canada with equal success in preventing the occurrence of paralytic poliomyelitis, and either may be used in the following schedules.

Modifications of the recommended schedule may be necessary because of missed appointments or intercurrent illness. Interruption of a recommended series does not require starting the series over again, regardless of the interval elapsed.

Table 1
Routine Immunization Schedule
for Infants and Children

Age	Immunization Against			
2 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis
6 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis ¹
12 months	Measles	Mumps	Rubella ²	
18 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4-6 years	Diphtheria	Pertussis	Tetanus	Poliomyelitis
14-16 years	Diphtheria ³		Tetanus ³	Poliomyelitis ¹

Table 2**Immunization Schedules for Children Not Immunized in Early Infancy**

For Children 1 through 6 Years of Age

Timing	Immunization Against			
First visit ⁴	Diphtheria	Pertussis	Tetanus	Poliomyelitis
Interval after 1st visit				
1 month	Measles	Mumps	Rubella ²	
2 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis
4 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis ¹
16 months	Diphtheria	Pertussis	Tetanus	Poliomyelitis
Pre-school — See Note 5 following.				
At Age				
14-16 years	Diphtheria ³		Tetanus ³	Poliomyelitis ¹

For Children 7 Years of Age and Over

First visit ⁴	Diphtheria ³		Tetanus ³	Poliomyelitis
Interval after 1st visit				
1 month	Measles	Mumps	Rubella ²	Poliomyelitis ¹
2 months	Diphtheria		Tetanus	Poliomyelitis
14 months	Diphtheria		Tetanus	Poliomyelitis
10 years	Diphtheria		Tetanus	Poliomyelitis ¹

Notes:

1. This dose may be omitted if live (oral) polio vaccine is being used.
2. Rubella vaccine is also indicated for all girls and women of childbearing age who lack proof of immunity. At all medical visits the opportunity should be taken to check whether girls and women have received rubella vaccine.
3. Diphtheria and Tetanus Toxoid (Td), a combined adsorbed "adult type" preparation for use in persons 7 years of age or more, contains less diphtheria toxoid than preparations given to younger children and is less likely to cause reactions in older persons.

4. Measles, mumps and rubella vaccines may also be given at the first visit if it is considered likely that a child will not return for further immunization. It has not been shown however, that full response to all antigens will occur.

5. When the last of the above doses are given before the 4th birthday, consideration should be given to administration of an additional dose at school entry.

B. Immunization for Adults

Prevention of infection by means of immunization is a life-long process which should be tailored to meet individual variations in risk resulting from occupation, foreign travel, underlying illness, lifestyle, etc. The following table lists approved vaccines which may be indicated for use in adults. All Canadian adults require maintenance of immunity to tetanus and diphtheria, preferably using combined (Td) toxoid. Persons over 65 years of age should receive influenza vaccine annually. Recommended immunizations for health care workers are detailed separately.

Teenagers and young adults require special attention. Some may not have received recommended vaccines while others may have received inadequate or less immunogenic vaccines (e.g. killed measles vaccine). Still others may be unprotected as a result of inappropriate or incorrect procedures (e.g. concurrent administration of immune globulin with live virus vaccines, live measles vaccine given before 1 year of age, improper storage, etc). Despite the success of recent childhood immunization programs, measles and rubella viruses continue to circulate among susceptible young adults. Given the infrequency with which this group seeks medical care, practitioners and health officials should utilize every opportunity to review and upgrade their protection.

Adults will usually respond adequately to vaccines unless they are immunocompromised. As with children, a single injection of most live virus vaccines will provide durable protection while inactivated vaccines and toxoids produce a lesser degree of immunity after a single dose; for adequate and sustained protection, repeated doses at appropriate intervals are usually necessary. Intervals for

adults receiving a primary series are generally the same as for children. Intervals for booster doses required to maintain protection are indicated in the table.

Immunization for Adults

VACCINE OR TOXOID	INDICATION	FURTHER DOSES
BCG (24)	High risk exposure	None
CHOLERA (27)	If required for foreign travel	Every six months*
DIPHTHERIA (29) (adult preparation)	All adults	Every 10 years preferably given combined with tetanus toxoid as Td
HEPATITIS B (34)	High risk exposure	Unknown
INFLUENZA (40)	High risk adults and all persons over 65 years	Every year using current vaccine formulation
MEASLES (43)	All persons born after 1956 who are susceptible to measles	None
MENINGOCOCCAL (49)	High risk exposure	Unknown
MUMPS (51)	Young adults with no history of mumps	None
PERTUSSIS (53)	Not indicated	
PLAGUE (56)	High risk exposure	See page 57
PNEUMOCOCCAL (58)	Conditions with increased [†] risk of pneumococcal disease	None
POLIOMYELITIS (60)	Travel to endemic area or other exposure risk	See pages 62-64, 102
RABIES (65) Pre-exposure use	Occupational or other risk	Every two years* See page 72
RUBELLA (73)	Susceptible women of childbearing age and certain male health care workers	None
TETANUS (78)	All adults	Every 10 years
TYPHOID (81)	High risk exposure	Every 3 years*
YELLOW FEVER (83)	Travel to endemic area or if required for foreign travel	Every 10 years*

*While risk continues

() Indicates pages where details of vaccination are presented.

Part 3

Active Immunizing Agents

BCG Vaccine

Mortality and morbidity from tuberculosis have declined significantly in Canada in the last few decades. The incidence of tuberculosis varies from one geographic region to another and is highest in native (Indians, Inuit and Métis) populations, in older age groups (particularly males) and in immigrant groups from countries with a high incidence of the disease.

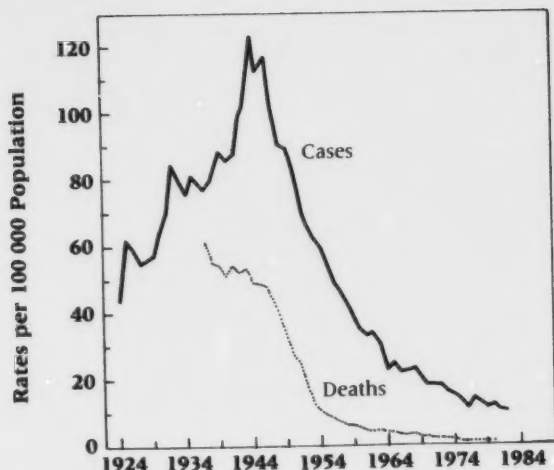
Major control measures practised in Canada include efforts to establish an early diagnosis, adequate treatment of active cases and use of preventive chemotherapy in individuals considered to be at high risk of developing active disease. BCG vaccination is only used for selected population groups.

Preparations Used for Immunization

Bacille Calmette-Guérin vaccine (BCG) is a suspension of a live attenuated strain of *Mycobacterium bovis*. It is available as a lyophilized culture either for intradermal or for percutaneous use. The intradermal preparation of BCG vaccine is recommended because the dose administered is less subject to variation. **Intradermal and percutaneous preparations are NOT interchangeable** and the manufacturer's instructions must be followed carefully. For infants under 12 months of age, a reduced dose, usually one-half of the adult dose, is recommended.

There are many BCG vaccines available in the world today; all are derived from the original strain but they vary in immunogenicity, efficacy and reactogenicity. Vaccines currently available in Canada have been evaluated only for their ability to produce a positive tuberculin reaction. Results of controlled trials in several countries using other vaccines have shown a reduction ranging from none to 80% in the incidence of clinical tuberculosis. The protective efficacy is apparently much higher in developed compared with developing countries. The protection conferred is relative in degree but may last for 15 years or more.

**Tuberculosis:
Reported Cases, 1924-1982
and Deaths, 1937-1981, Canada,
Rates per 100 000**



Vaccine should be protected from heat and direct sunlight and stored according to the manufacturer's instructions, usually at less than 5°C. Reconstituted freeze-dried vaccine should be discarded if not used within 48 hours.

Recommended Usage

BCG vaccine should be considered for use in Canada only in the following persons or groups:

- 1) individuals who are repeatedly exposed to untreated or inadequately treated active tuberculosis;
- 2) communities or groups of persons with high rates of infection, including Indian, Métis and Inuit children, in which other control measures have proved ineffective;

3) health workers at considerable risk of exposure to unrecognized infectious pulmonary tuberculosis or who handle tubercle bacilli or potentially infectious specimens in a laboratory;

4) newborn infants whose mothers have infectious tuberculosis at the time of delivery, although isoniazid (IHN) prophylaxis is preferred to avoid the necessary separation of mother and infant when BCG is used. However, BCG is recommended if the infecting strain is INH resistant or if compliance with a program of INH prophylaxis cannot be assured. BCG may also be considered for the infant after INH prophylaxis is completed, provided chest radiographs and tuberculin test are negative.

BCG vaccine should be given only to persons with a negative tuberculin skin test (Mantoux) to a PPD which is bioequivalent to 5 TU PPD-S. Infants under 6 weeks of age need not be tuberculin tested before receiving BCG.

Following intradermal injection, the development of erythema, papule formation, and sometimes superficial ulceration in 3 to 6 weeks usually indicates successful vaccination. Some enlargement of the regional lymph nodes usually accompanies the lesions at the vaccination site. Most authorities believe the development of a typical pustule and scar at the vaccination site indicate that protection has been conferred even if conversion to positive of the tuberculin skin test (5 TU) cannot be demonstrated. In these cases vaccination need not be repeated.

There is no evidence to indicate that revaccination is necessary after successful BCG vaccination. It should be noted that certain viral infections, particularly measles, may diminish or transiently abolish tuberculin sensitivity.

Adverse Reactions

Adverse reactions are more common in young vaccinees and are frequently related to improper technique in administration. These reactions are generally mild, but moderately severe and, very rarely, severe or even fatal reactions can occur. Such incidents appear to vary with the strain of vaccine, dose and method of vaccination and with the age or race of the recipient. Mild reactions include

persistent or spreading skin ulceration, inflammatory adenitis and keloid formations. These may occur in up to 5% of patients.

Moderately severe reactions such as suppurative adenitis occur at a rate of 0.1% and are responsive to anti-tuberculous therapy.

Severe osteitis and generalized BCG infection occur very rarely (1 in about 1 000 000 vaccinations).

Contraindications

BCG vaccination is contraindicated for persons with a positive tuberculin skin test, with impaired cell-mediated immune response or with extensive active skin disease or burns. BCG should not be given within 4 weeks of administration of measles and mumps vaccine since these are known to suppress the tuberculin reaction.

Vaccination of pregnant women should preferably be delayed until after delivery, although no harmful effects on the fetus have been observed.

Other Considerations

BCG vaccine does not provide permanent or absolute protection against tuberculosis, and this disease should be considered as a possible diagnosis in any vaccinee who presents with suggestive history, signs or symptoms. It is difficult to differentiate between a positive tuberculin test due to BCG and that resulting from active tuberculosis infection. Caution should be observed in attributing tuberculin positivity to BCG vaccination, particularly in persons who have been exposed to active disease.

Cholera Vaccine

Cholera is an acute diarrheal disease caused by an enterotoxin produced by *Vibrio cholerae*, both the classical and El Tor biotypes. Mortality ranges from over 50% without treatment to less than 1% in adequately treated patients. Since 1960, epidemics have occurred in Southern Asia, Africa and Europe. There is a small focus of cholera in the U.S.A. on the Gulf of Mexico coast. Infection is generally acquired from contaminated water or food. The El Tor biotype survives in the environment more readily than the

classical type and a higher incidence of asymptomatic carriers occurs.

Only 7 cases have been reported in Canada since 1945, all acquired in foreign countries. Risk of an outbreak in a country with modern sanitation and water supplies is very low.

Preparations Used for Immunization

Cholera vaccine consists of a killed, phenol-preserved mixed suspension of the Inaba and Ogawa serotypes of *Vibrio cholerae*. Both serotypes are included because there is not full cross-protection between them. The vaccine is equally effective against both the classical and El Tor biotypes, which are antigenically identical. A full course of vaccine is believed to prevent clinical cholera in about half the recipients for 3 months or longer, but protection is minimal or non-existent a year after the last dose. Asymptomatic carriage of *Vibrio cholerae* is not prevented.

Recommended Usage

Cholera vaccine is not routinely recommended for travelers unless countries require a certificate of vaccination as a condition of entry. Persons following the usual tourist itinerary in countries affected by cholera are at virtually no risk of infection. *Cholera vaccination does not prevent people from becoming asymptomatic carriers and therefore is not recommended for controlling the spread of infection or in management of contacts of imported cases.* Although a certificate of cholera vaccination is not required for any country under the International Health Regulations and cannot be justified epidemiologically, some countries still insist on cholera vaccination having been performed 6 or more days before entry. Up-to-date details of such requirements, which vary frequently, are available from local health departments.

A single dose of vaccine is generally sufficient if given merely to satisfy the requirements of those countries still requiring proof of vaccination. Primary immunization usually consists of 2 injections about 4 weeks apart. Booster doses are recommended every 6 months as long as likelihood of infection exists. Primary immunization need never

be repeated for booster doses to be effective. Vaccine is not recommended for infants under 6 months of age.

When both yellow fever and cholera vaccines are required, they are preferably given 3 or more weeks apart to avoid mutual interference with antibody responses. No interference with protection has been demonstrated, however, and they may be given simultaneously when circumstances make it necessary.

Adverse Reactions and Contraindications

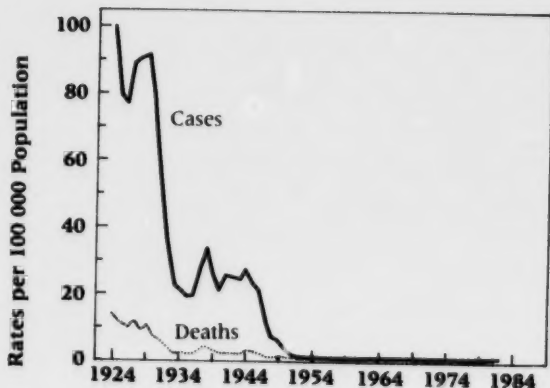
Serious reactions to cholera vaccination are very rare but, when they do occur, constitute a contraindication to further

Diphtheria Toxoid

Diphtheria is a serious communicable disease, caused by toxigenic strains of *Corynebacterium diphtheriae*. The mortality is up to 10% in untreated susceptible persons, with high death rates in the very young and the elderly. The organism may be harboured in the nasopharynx, skin and other sites of asymptomatic carriers, making eradication of the disease difficult.

In Canada the reported annual incidence of diphtheria has decreased progressively and markedly during the past 50 years. Routine immunization against diphtheria in infancy and childhood has been widely practised for the past 40 years. This has resulted in a remarkable decline in the morbidity and mortality of this disease. In 1924, there were 9000 cases reported, but only 11 cases were reported in 1982. However, toxigenic strains of diphtheria bacilli are still detected each year in considerable numbers of diphtheria carriers (pharyngeal, skin and ear) in Northern and Western Canada. Asymptomatic carriage of *C. diphtheriae* is far more common than clinical diphtheria. The disease occurs most frequently in unimmunized or partially immunized individuals. Although occasional cases of mild clinical diphtheria do occur in apparently fully immunized persons, antitoxin produced by immunization persists at protective levels for 10 years or more.

**Diphtheria:
Reported Cases, and Deaths,
Canada, 1924-1982,
Rates per 100 000**



Diphtheria toxoid introduced in 1926

Preparations Used for Immunization

Diphtheria toxoid is a cell-free preparation of diphtheria toxin treated with formaldehyde to detoxify it without affecting its antigenicity. The immunity conferred is antitoxic, not antibacterial, and thus protects against the potentially lethal systemic effects of diphtheria toxin but not directly against local infection.

Diphtheria toxoid is available as fluid (non-adsorbed) toxoid or combined with aluminum phosphate in preparations designated "adsorbed". Adsorbed toxoid induces higher antitoxin titres and more durable protection than

fluid toxoid and is recommended for routine use. In combined preparations containing pertussis vaccine, the immunogenic effects of the diphtheria toxoid is enhanced (an adjuvant effect). The amount of toxoid present in preparations is measured in flocculating units (Lf).

The toxoid is available alone or in combinations with tetanus toxoid, pertussis and poliomyelitis vaccines as listed in the Appendix. Note that combined preparations of diphtheria and tetanus toxoids do not all contain the same quantity of diphtheria toxoid. Preparations with smaller amounts of diphtheria toxoid (the most commonly used of which is designated Td) are intended for use in persons 7 years of age or more.

Recommended Usage

Routine immunization against diphtheria is recommended for all persons.

For primary immunization of children under the age of 7 years, it is preferable to use products in which diphtheria toxoid is combined with pertussis vaccine and tetanus toxoid (DPT), with the optional addition of inactivated poliomyelitis vaccine (DPT-Polio). The primary immunizing course of diphtheria toxoid alone or in combination consists of four doses and should ideally begin at 2 months of age. (See Part 2: Recommended Immunization Schedules). The time interval between the initial three doses should be a minimum of 4 weeks, and preferably 8 weeks; the fourth dose should be given one year after the third dose. Booster doses should be given at 4 to 6 years (school entry). A further booster dose of adult-type preparation (Td) should be given 10 years later.

The dose and route of administration vary with the product and the manufacturer's package insert should be consulted. **Adsorbed vaccines must be injected intramuscularly.**

For primary immunization of persons 7 years of age or older, the preferred agent is a combined adsorbed tetanus and diphtheria preparation (Td, adult-type preparation) containing less diphtheria toxoid than preparations given to younger children. This is less likely to

cause reactions in older persons. Two doses are given at least 8 weeks apart, with a further dose one year later to complete the course.

Adults should be given a booster dose of an adult-type preparation every 10 years; a combined preparation with tetanus toxoid (Td) is preferred unless there are contraindications to the administration of tetanus toxoid. If an adsorbed adult-type preparation is to be used, a prior Schick test or sensitivity test is unnecessary.

In addition to the measures outlined on page 89, close contacts (household, classroom or similar) of diphtheria cases should be given a dose of a toxoid preparation appropriate for their age unless they are known to be fully immunized with the last dose within 10 years. The remaining doses required to provide full immunization should be given to any contacts who were previously unimmunized or incompletely immunized.

Patients convalescent from diphtheria should be given a complete primary course of toxoid since diphtheria infection does not always confer immunity. A clinical history of diphtheria is no justification for the withholding of immunization.

Adverse Reactions

Life-threatening reactions to diphtheria toxoid are extremely rare. Diphtheria toxoid may cause severe but transient local and febrile reactions in older children and adults, the frequency increasing with age, the dose of toxoid, and the number of doses given.

Contraindications and Precautions

Persons 7 years of age or older should only be given preparations formulated for older children and adults. Before giving a combined vaccine, particularly one containing pertussis vaccine, it is most important to ensure that there are no contraindications to the administration of any of the other components.

When a combined diphtheria-tetanus preparation is being considered, care should be taken to avoid administration of tetanus toxoid more frequently than is recom-

mended (see section on Tetanus Toxoid) or adverse reactions may result.

Combined Vaccines Against Diphtheria, Pertussis, Tetanus, and Poliomyelitis

Diphtheria and tetanus toxoids and pertussis vaccines are most often administered as a combined product (DPT). A combination that also includes inactivated poliomyelitis vaccine is available (DPT-Polio). Combined vaccine preparations adsorbed with aluminum salts are significantly more immunogenic for all components than are the fluid (non-adsorbed) DPT and DPT-Polio formerly used widely in Canada. Accordingly, adsorbed DPT or DPT-Polio is preferred.

Whereas fluid vaccines are administered subcutaneously, **adsorbed vaccines must be administered intramuscularly** to minimize the degree of local reaction. Use of the vaccines should be in accordance with the manufacturer's instructions.

Local and systemic reactions after DPT or DPT-Polio appear to be due primarily to the pertussis component (see Pertussis section). Reaction rates of the combined vaccines are similar to those of pertussis vaccine alone. Following serious reactions it may be necessary to continue immunization with individual agents or combinations without pertussis vaccine.

The combined adsorbed preparation of diphtheria and tetanus toxoid formulated for adults (Td) is the preferred immunizing agent for persons aged 7 years or more. It is recommended for

- a) primary immunization of older children and adults against diphtheria and tetanus;
- b) regular booster doses for children at 14 to 16 years of age and every 10 years to adults; and
- c) management of wounds when tetanus toxoid is indicated.

For details of usage and precautions to be taken, see relevant sections of the Guide.

The use of fractional doses in an attempt to reduce the severity of adverse reactions cannot be recommended be-

cause there is no evidence of the safety or efficacy of such smaller doses.

Hepatitis B Vaccine

Hepatitis B virus (HBV) is one of several viruses that cause hepatitis. HBV is a double stranded DNA virus with three major antigens known as surface (HBsAg), e (HBeAg), and core (HBcAg). Hepatitis B virus vaccine containing purified HBsAg induces antibody (anti-HBs) to surface antigen and confers immunity to hepatitis B.

The viral particle is present in the blood of patients with hepatitis B and of chronic carriers. It has also been detected in various body secretions of infected patients, including saliva, urine, semen and vaginal secretions. Attempts to cultivate the virus in cell cultures and small laboratory animals have not been successful. HBV has been propagated in primates, notably chimpanzees.

Infection is usually associated with exposure to blood or blood products, the virus being transmitted by percutaneous or permucosal routes.

HBV infection may be inapparent or may result in acute or chronic disease. Acute illness may last up to 3 months. In about 10% of patients, the disease progresses to a chronic form: 7% develop chronic persistent hepatitis, a relatively mild disease characterized by persistent antigenemia and minimal liver involvement; 3% develop chronic active hepatitis, a more severe disease which may or may not be associated with antigenemia.

HBsAg is present in blood during acute infection and early convalescence. Chronic antigenemia, the carrier state, may develop, especially in immunocompromised patients, in those infected at a young age, and in certain ethnic groups. It may be as high as 90% in those infected in the neonatal period. Chronic carriers often do not have overt liver disease but in the long term are at increased risk of hepatic cirrhosis and hepato-cellular carcinoma. Chronic HBsAg carriers are potentially infectious and are an important source of infection.

Hepatitis B Virus Infection in Canada

The precise number of infections occurring in Canada is not known. Over 1000 cases have been notified annually in recent years but it is likely that there were many unreported cases. Carriage rates of HBsAg in Canadian blood donors of about 0.15%, and in patients in a general hospital of 0.8%, have been reported. Recent immigrants from South-East Asia have rates of up to 11%. Presence of anti-HBs in the blood is an indicator of past HBV infection. Limited surveys have shown that less than 5% of Canadian residents possess anti-HBs, and Canada may be regarded as a country with low HBV prevalence. Antibody prevalence varies within Canada, however, and is significantly higher in certain immigrant populations, in certain occupational categories, and in some regions. Canadian data are limited and reported prevalence rates are not necessarily representative of those that may exist in all hospitals, institutions or locations in Canada. From published and unpublished data made available to the Committee, the prevalence of HBV markers in various population categories is estimated to be as follows: high (HBV markers often exceeding 20%) in homosexually active men, pathologists and laboratory technologists engaged in biochemistry and hematology, users of illicit injectable drugs, dialysis unit staff, hemophiliacs, residents of institutions for the mentally retarded, and immigrants from South-East Asia; intermediate (markers generally 7 to 20%) in hospital nurses, laboratory technologists other than those in the high prevalence category, staff of institutions for the mentally retarded, and dentists; low (markers less than 7%) in administrative hospital staff, medical and dental students, blood donors and other healthy adults. These prevalence categories are a guide for the initial planning of immunization programs.

Preparations Used for Immunization

The vaccine consists of purified, formalin inactivated alum-adsorbed surface antigen of hepatitis B virus (HBsAg) prepared from plasma of human carriers. A unique feature is that the antigenic material is not derived from microorganisms propagated in the laboratory but directly from human

material. During preparation the vaccine undergoes various physical and chemical procedures which remove non-surface antigens of HBV, serum proteins and other infectious agents which may have been present in the initial plasma pools. The vaccine is subsequently tested in cell cultures for other detectable viruses and in susceptible chimpanzees for hepatitis viruses. The vaccine stimulates antibody (anti-HBs) to surface antigen but does not induce antibodies to other antigens of HBV or to serum or blood group antigens.

Seroconversion rates for anti-HBs of 90 to 95% have been observed in healthy infants over 3 months of age, children, and adults. Antibody response is poorer in immunocompromised patients and those on renal dialysis and decreases somewhat with increasing age of the vaccinee. Concurrent administration of hepatitis B immune globulin, however, does not interfere with the antibody response to vaccine. Antibodies persist for at least 3 years following completion of the full immunization schedule, but the duration of immunity and need for boosters are not yet known. In field trials in the United States, protection against illness was complete for persons who developed anti-HBs after a course of vaccine. Antigenic subtypes of HBV exist, but immunization confers immunity to all subtypes.

The vaccine should be stored at 2 to 8°C. **Vaccine must not be frozen.**

Recommended Usage

Vaccine is not recommended for general use, but should be considered for persons and groups who are at substantially greater risk of HBV infection than the general population. Primary immunization requires three intramuscular doses of vaccine. The second and third doses should be given 1 and 6 months after the first dose. Each dose should contain 20 µg HBsAg protein for adults, 10 µg for infants and children less than 10 years of age, and 40 µg for immunocompromised patients. The need for subsequent booster doses is not yet known.

Seroconversion rates exceed 90% in healthy persons, so post-immunization serological testing is not indicated except in persons whose subsequent management depends upon knowledge of their immune status and in those categories of persons in whom a diminished antibody response is possible, e.g. immunocompromised persons or those on renal dialysis.

Vaccine should be given only to those who are at increased risk of hepatitis B infection, namely, persons who are exposed frequently to blood, blood products or to body secretions which contain the virus. Experience with this new vaccine is limited, and only preliminary recommendations for its use can be made at present. These should be regarded as current guidance for the best use of the vaccine and may be expected to be modified as further knowledge accumulates. Given below is a list of persons, not necessarily in order of priority, who are considered to be at increased risk and who are therefore potential vaccine recipients:

- Certain Categories of Patients:
 - those receiving repeated injections of certain blood products (Factor VIII or IX concentrates) and lifetime recipients of multiple blood transfusions,
 - patients on renal dialysis,
 - infants born to HBsAg positive mothers whose contact with a carrier mother will continue. (p. 38):
- Health Care Workers and Students Repeatedly Exposed to Blood or Blood Products. These may include:
 - operating room personnel,
 - emergency room and ambulance staff,
 - IV teams,
 - laboratory personnel,
 - blood bank staff,
 - staff on oncology, nephrology and hepatology units,
 - pathologists and morgue attendants,
 - surgeons,
 - dentists, dental assistants and hygienists;
- Certain Staff and Residents of Institutions for the Mentally Retarded. Those in contact with aggressive, biting residents are at highest risk;
- Homosexually Active Males;

- Users of Illicit Injectable Drugs;
- Sexual and Household Contacts of Carriers;
- Embalmers.

Since the risk of exposure varies in different settings, it is recommended that institutions or jurisdictions review their own situation in order to develop their own priorities for immunization. Hospital employees who have no contact with blood or blood products are at no greater risk than the general population.

Whenever possible, persons for whom vaccine is recommended should be vaccinated before or as soon as possible after they become exposed to the increased risk. An example would be students entering certain health professions.

Post-exposure Use

a) Newborn Infants

Pregnant women in population groups known to have high carrier rates should be screened for HBsAg because of the high risk of infection in infants born to mothers infected with HBV. Infants born to HBsAg positive mothers should be given hepatitis B immune globulin immediately at birth. Such infants should also receive three 10 μ g doses of hepatitis B vaccine beginning as soon as possible after birth with subsequent doses one and six months after the first (see page 91 for a more complete description).

b) Needlestick or Similar Exposure

Persons who have percutaneous or mucous membrane exposure to HBsAg positive blood products and who are at possible risk of further exposure should begin a course of hepatitis B vaccine at the same time or as soon as possible after receiving HBIG (see page 90). If vaccine is begun within one month of administration of the first dose of HBIG, the second dose of HBIG normally recommended need not be given.

c) Sexual Contacts of Acute Cases of Hepatitis B

Persons having continuing sexual exposure to a case of acute hepatitis B in whom HBsAg antigenemia persists for more than 3 months should, in addition to prophylaxis with HBIG as described on page 92, be given a course of

vaccine, which may be begun at the same time as the second dose of HBIG is given.

Prevaccination Serological Screening for Antibody

Serological testing to determine the state of immunity of potential vaccinees is not necessary for medical reasons and is only cost effective in populations in which a substantial proportion of persons have anti-HBs and consequently do not need the vaccine.

Screening in groups with the highest risk of HBV infections such as users of illicit injectable drugs, homosexually active males, and institutionalized mentally retarded persons will be cost effective unless testing costs are extremely high. For groups at intermediate risk, such as health care workers with an expected prevalence of 7 to 20%, screening may only be marginally cost effective and not considered worthwhile. For groups with a low expected prevalence of HBV serologic markers, such as persons entering health professions, screening would not be cost effective.

For screening purposes a test for anti-HBs will generally be sufficient.

Adverse Reactions and Contraindications

Side effects reported among vaccine recipients to date have all been mild and transient and generally limited to soreness and redness at the injection site.

Pregnancy should not be considered a contraindication to use of this vaccine for persons in whom it is otherwise recommended. Data are not available on the safety of the vaccine for the fetus, but since it is an inactivated vaccine the risk may be expected to be negligible. HBV infection in a pregnant woman may result in severe disease for the mother and chronic infection in the infant.

Neither adverse reactions nor beneficial effects have been observed when vaccine has been given to immune persons or carriers.

No documented cases of Acquired Immunodeficiency Syndrome (AIDS) have been attributed to the vaccine. Although the vaccine is produced from human blood, the

procedures used in the preparation of the vaccine are considered adequate to eliminate the putative etiologic agent.

Influenza Vaccine

Influenza is caused by influenza A and B viruses and occurs in Canada almost every year, generally during the winter months. Its annual incidence varies widely. Influenza A viruses, which periodically undergo antigenic change, are the most common cause of epidemic influenza whereas influenza B viruses more often cause local outbreaks, particularly in institutions. Persons at greatest risk of serious disease and death are the chronically ill and elderly. It should be noted that many cases of so-called "influenza" illness, especially during non- epidemic years, are not caused by influenza viruses.

Influenza A viruses are classified into subtypes based on their hemagglutinin (H) and neuraminidase (N) antigens. Recently circulating strains have possessed one of three H and one of two N antigens, and the subtypes are designated accordingly (e.g. H3N2; H1N1). Antibodies to these antigens, particularly to H antigen, confer immunity to a virus carrying the same antigen. Pandemic influenza is usually associated with a major antigenic change or "shift", the pandemic virus having a different H, and often a different N, antigen from strains circulating previously. During inter-pandemic periods, minor H antigen changes ("drift") are common, and the greater the change the less will be the immunity conferred by the previously circulating virus to the new strain. The antigens of influenza B viruses are much more stable than those of influenza A viruses although antigenic variation does occur.

Canada, like other countries, has been affected by major influenza pandemics, which are characterized by rapid global spread associated with a major antigenic shift in influenza A virus antigens, e.g. in 1889-90, 1918-19 and 1957-58. Major epidemics of influenza A associated with smaller antigenic changes have also occurred. Outbreaks of influenza B are generally more localized and in any one year may be restricted to one region of the country. An

association between influenza outbreaks, especially those caused by type B virus, and cases of the rare but serious Reye's syndrome has been noted.

Preparations Used for Immunization

Influenza virus vaccine available in Canada is a suspension of one or more strains of inactivated virus that have been cultivated in embryonated hens' eggs and purified by zonal centrifugation.

The virus strains chosen for inclusion in influenza vaccine are changed from time to time to ensure that they include antigens that are expected to provide the best protection during the following winter.

Vaccines are available as "whole-virus" or as "split-virus" preparations. Reactions such as local pain and fever are more common from whole-virus preparations, particularly in children. Split-virus vaccines are prepared from virus that has been disrupted by organic solvents or detergents and are less likely to cause side effects. For this reason, they are recommended for children. For persons who have not been exposed to a strain against which protection is sought, two doses of vaccine four or more weeks apart may be necessary, and for information in this regard reference should be made to the manufacturer's package insert and to the current annual recommendations of the Committee.

Inactivated influenza A vaccine confers about 70% protection during the year after its administration. Low levels of protection may persist for a further one to two years if the prevalent strain remains the same or has only minor antigenic "drift". There is little or no cross protection to a new strain when major antigenic changes (antigenic "shift") have occurred.

Recommended Usage

The Committee issues **annual statements** on the composition and usage of influenza vaccines and these **should be consulted for current details**. Influenza vaccines usually contain both influenza A and influenza B virus strains.

Annual influenza vaccination each fall is advised for the following persons who are considered most likely to suffer severe illness or death from influenza infection:

- a) Persons of any age who have such conditions as
 1. acquired or congenital heart disease associated with pulmonary congestion
 2. chronic pulmonary disease associated with compromised respiratory function
 3. chronic renal disease, especially with azotemia
 4. chronic metabolic disease such as diabetes mellitus
 5. immunodeficiency or immunosuppression, including malignant tumors, leukemia, etc. under therapy
 6. chronic severe anemias such as sickle cell disease.
- b) Older persons, particularly those over 65 years of age.

In considering vaccination of persons who provide essential community services or who may be at increased risk of exposure, such as medical care personnel, the inherent benefits, risk and cost of vaccination should be taken into account.

One dose of whole-virus or split-virus inactivated influenza vaccine, or for previously unimmunized children two doses of split-virus vaccine, should be administered in the dosage and by the route recommended by the manufacturer. Immunization is best given before the end of November each season, and should be repeated annually for those at high risk as indicated above.

Intradermal administration of influenza vaccine cannot be generally recommended since the serological response is unpredictable especially in those having no prior experience with the strain concerned.

Adverse Reactions

Fever, malaise and myalgia may occur within a day or two after vaccination, their incidence being highest in children, particularly when whole-virus vaccine is used.

Since 1976, no association of Guillain-Barré Syndrome with influenza vaccination has been observed although in that year an increased incidence of this condition (10 cases per million persons vaccinated) occurred within 10 weeks following administration of swine influenza virus vaccine.

Contraindications and Precautions

Individuals with hypersensitivity to eggs should not be given influenza vaccine. Allergic responses are very uncommon and are probably a consequence of exquisite sensitivity to some vaccine component, most likely residual egg protein which is present in minute quantities.

When considering influenza immunization for pregnant women, the same criteria should be used as are applied to other persons. Physicians prudently limit prescription of drugs, including biologics, for pregnant women. However, no evidence has been presented to suggest that influenza vaccination of pregnant women poses any maternal or fetal risk. Furthermore, because influenza vaccine is an inactivated viral preparation, it does not have the theoretical risks that impel caution in the use of live virus vaccines.

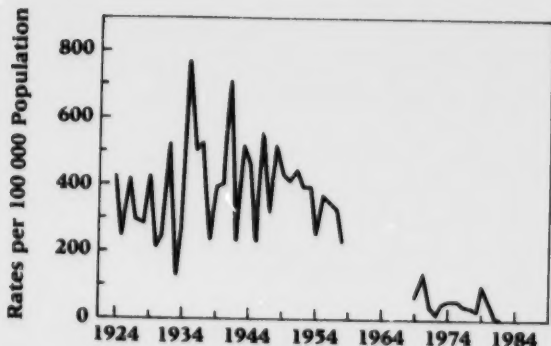
Measles Vaccine

Introduction

Measles (rubeola) has a worldwide distribution and remains a serious disease despite a reduction in incidence in those countries where vaccine has been widely used. Complications such as otitis media and bronchopneumonia occur in about 10% of cases and are more common in poorly nourished, chronically ill and very young children. Measles encephalitis occurs in approximately 1 of every 1000 reported cases and may result in mental retardation. Death is estimated to occur once in 3000 cases. Furthermore, natural measles infection is implicated in the etiology of sub-acute sclerosing panencephalitis (SSPE), a fatal disease.

Measles can be effectively controlled by vaccination of all susceptible persons. Before the introduction of vaccine, measles occurred in cycles with an increased incidence every 2 to 3 years. After the introduction of the vaccine, the incidence declined and was accompanied by a reduction in the number of deaths and of complications. Transmission of measles virus has been effectively interrupted in several jurisdictions in Canada and the incidence of measles is at an all time low — making elimination a practical goal for the country as a whole.

**Measles:
Reported Cases,
1924-1982*
Rates per 100 000**



Measles live vaccine licensed in 1963

Measles killed vaccine licensed in 1964

*Measles was not nationally reportable 1959-1968

Preparations Used for Immunization

Live measles virus vaccine is prepared from a "further attenuated" virus derived from the original Edmonston B strain. It is available alone, in combination with rubella vaccine, or in combination with rubella and mumps vaccines.

In clinical trials, the live vaccine has produced over 95% seroconversion, although the antibody titres achieved are less than those following natural disease. As with natu-

ral disease, antibodies remain detectable for more than 15 years. In certain closed populations where measles has not occurred since the administration of vaccine, antibody levels have persisted for many years; and in immunized individuals whose antibody titres have dropped below detectable levels, re-challenge with vaccine produces a booster-type response.

Failure of protection against measles may result from the administration of improperly stored vaccine. Since 1979, a new stabilizer incorporated into the vaccine makes it more resistant to inactivation by heat. However, proper refrigeration, storage and handling are still important to prevent loss of potency.

Recommended Usage

A single dose of live measles vaccine, preferably combined with rubella and mumps (MMR), is recommended routinely for all children on, or as soon as practicable after, their first birthday. Measles vaccine is also recommended for children and adolescents who have no record of having had measles diagnosed by a physician, or who received live attenuated vaccine *before* the age of 12 months, or who are known to be seronegative. Routine primary immunization of adults born before 1957 is not necessary because they are very likely to have acquired immunity by natural infection. Immunization within 72 hours of exposure to measles is not known to produce adverse effects and will usually prevent measles.

When an infant under the age of one year is at high risk of exposure to natural measles, immunization may be considered as early as 6 months of age. Preferably, however, infants should be given immune globulin prophylaxis at the time of exposure (see page 87). Infants given the vaccine during the first year of life should be revaccinated at 12 to 15 months of age to ensure lasting immunity.

Revaccination should be considered for all children previously given:

- a) live measles vaccine before 12 months of age;
- b) killed measles vaccine at any age whether given alone or

followed by live measles vaccine within 2 years (see page 47);

c) further-attenuated live measles vaccine and human immune globulin (IG), simultaneously; and

d) live attenuated measles vaccine within 3 months of receiving IG.

Adverse Reactions

The vaccine produces a mild, non-transmissible usually subclinical infection in persons to whom it is given. Fever, with or without rash, may be seen in about 15% of persons 5 to 12 days after administration of vaccine.

Encephalitis has been reported in association with administration of live attenuated measles vaccine (approximately 1 per million doses in North America), but its incidence is much lower than that observed with the natural disease (approximately 1 per thousand cases in the United States).

A small number of hypersensitivity reactions to measles vaccine have been reported in persons who on eating eggs suffer anaphylactic hypersensitivity manifested by hives, swelling of the mouth and throat, difficulty in breathing, hypotension and shock.

The risk of developing subacute sclerosing panencephalitis (SSPE) following measles vaccination is considerably less than the risk following natural measles infection. There has been a dramatic decline in the incidence of SSPE in the United States since the introduction of widespread measles immunization.

Precautions and Contraindications

As with all other live vaccines, measles vaccine is specifically contraindicated in any individual whose immune mechanism is impaired as the result of disease, injury or therapy as detailed on page 11. Because the vaccine virus is non-transmissible, it is desirable to immunize close contacts of immunocompromised individuals in order to minimize the risk of exposure of the latter to measles. While there is no known risk in giving measles vaccine during pregnancy, on theoretical grounds it is desirable to avoid giving live measles vaccine to pregnant women.

Tuberculosis may be exacerbated by natural measles infection, but there is no evidence that measles vaccine has such an effect.

Persons who on eating eggs suffer anaphylactic hypersensitivity manifested by hives, swelling of the mouth and throat, difficulty in breathing, hypotension and shock, should not be given measles vaccine. Such individuals may be identified by inquiry about the occurrence of ill effects on eating eggs. Persons who have egg allergies that do not result in anaphylactic symptoms and those with allergies to chickens or feathers may be vaccinated in the usual manner.

Since measles vaccine contains trace amounts of neomycin, persons who have experienced anaphylactoid reactions to topically or systemically administered neomycin should not receive measles vaccine.

Persons Previously Given Inactivated Measles Vaccine

Inactivated measles vaccine was available in the 1960s in Canada and was used routinely in some jurisdictions, sometimes in conjunction with a dose of live vaccine given within the following 3 months. Some children immunized with killed vaccine who were subsequently infected with wild measles virus developed an atypical measles syndrome with high fever, a rash that was sometimes purpuric, and severe respiratory involvement.

Children who received inactivated vaccine alone or inactivated vaccine followed by live measles vaccine in the following 2 years should be revaccinated with live vaccine in the hope of preventing atypical measles syndrome. The degree of protection that will be conferred is uncertain, and there is the possibility of severe local reactions at the site of injection of the live vaccine; but serious illness is much more likely to occur following natural infection with measles virus than after administration of live vaccine.

Elimination of Measles in Canada

Elimination of measles in Canada is a desirable and feasible goal. Since the introduction of measles vaccine in Canada in 1963, there has been a remarkable reduction in reported

measles incidence, but local epidemics have continued to occur. Because an effective vaccine is available and because there is no non-human reservoir or source of infection, measles elimination within a population is possible if high levels (greater than 95%) of immunization are maintained.

The major components of a measles elimination program include

- a) achievement and maintenance of high immunization levels and documentation of proof of immunity in the entire population at risk
- b) intensive surveillance and rapid reporting of all suspected measles cases
- c) prompt outbreak control measures designed to prevent spread from index cases to susceptible contacts.

To be successful, these measures require a high level of cooperation between all health professionals providing primary medical care in the community, and public health personnel.

Maintenance of high levels of immunization (more than 95%) requires strenuous efforts to immunize children as soon as possible after their first birthday, and documentary proof of immunity for all children on entry to day-care centres, schools or similar settings. Persons born before 1957 can be considered immune to measles. Immunity to measles in others can only be considered to exist in those persons who have documentation of 1) adequate immunization with live measles vaccine on or after the first birthday with the date of vaccination recorded; 2) measles diagnosed by a physician; or 3) serological evidence of measles immunity.

Intensive programs designed to immunize all children without documentary proof of measles immunity at day care, school entry or in later school years, even in the absence of mandatory measles immunization legislation, have achieved immunization rates of over 90% of the childhood population in some parts of Canada. In jurisdictions where such voluntary programs are not effective, legislation should be introduced to require documented proof of immunity to measles before a child may attend school.

To control outbreaks, all cases of suspected measles should be reported and investigated promptly. An outbreak should be considered to exist in any community in which even one confirmed case of measles occurs. Although serological confirmation is desirable, for practical purposes the following clinical case definition may be considered diagnostic of measles: 1. generalized rash of at least 3 days duration; 2. fever of 38.3°C or higher; 3. cough or coryza or conjunctivitis.

If measles is confirmed or suspected, there should be prompt investigation to determine the source of infection and to ensure protection of susceptible contacts through immediate active or passive immunization. Persons without documentation of immunity should be excluded from day-care centres, schools or similar settings until they receive vaccine or until 14 days after the date of onset of the last case of measles.

Because of the continued presence of measles elsewhere in the world, measles elimination programs will have to be maintained and supported until global eradication is accomplished. Persons travelling to countries where measles continues to occur should ensure they are immune prior to travel.

Meningococcal Polysaccharide Vaccine

Since 1980, the reported annual incidence of meningococcal disease in Canada has been about 200 cases (22% infants). Mortality has varied from 5% to 15%. Between 1977 and 1981 the average annual number of deaths reported was 32, about one quarter being infants.

Information on the prevalence in Canada of meningococcal serogroups is incomplete. Of 476 meningococci isolated from CSF and blood collected between 1979 and 1982, about half were Group B. In the past four years Group C has declined from about 25% to 14% and Group W-135 has risen from being rarely observed to 14%.

Preparations Used for Immunization

Meningococcal vaccines contain purified capsular polysaccharide. Products licensed in Canada are monovalent Group C vaccine, bivalent Group A and C vaccine, and a

quadrivalent vaccine containing Groups A, C, Y, and W-135.

Vaccines containing polysaccharides of Groups A and C have been shown to prevent meningococcal disease caused by the constituent groups among adults and children over 2 years of age both during civilian epidemics and in endemic disease in military populations. A single dose protects adults and older children for at least 2 years. No cross protection occurs between serogroups. In children under 2 years of age, two doses of monovalent Group A vaccine given 3 months apart have been shown to provide protection from epidemic disease for one year. If an epidemic persists, such children should be given a booster dose 1 year after the second dose. A single dose of Group C vaccine produces an antibody response but it has not yet been shown whether children under 2 years of age are protected from disease. In an epidemic, vaccine is indicated for persons of all ages over six months.

The serological response to vaccine containing polysaccharides of Groups Y and W-135 has not been established in individuals under 18 years.

Recommended Usage

Meningococcal vaccines are recommended for the control of outbreaks. Routine vaccination of civilians is not recommended. While no exact definition of a meningococcal "epidemic" exists, a cluster of cases in a delineated population should prompt consideration of vaccination of all residents at risk. Vaccine may also be considered for travellers intending to live for prolonged periods in countries with a high incidence of meningococcal disease. The quadrivalent vaccine should be used to prevent meningococcal disease in populations such as military recruits, who are clearly demonstrated to be at increased risk. If meningococcal disease due to any of the four serogroups occurs within a residential institution, use of the appropriate vaccine should be considered. Immunization of other populations can be justified only if the incidence of meningococcal disease approaches epidemic level.

Primary management of household contacts of cases of meningococcal disease should consist of chemoprophylaxis

and close surveillance. Rifampin is the agent of choice. In epidemics, meningococcal vaccines should be considered as an adjunct to chemoprophylaxis for household contacts. Since almost half of the secondary family cases occur more than five days after the primary case, there is often sufficient time for potential benefit from vaccination.

Adverse Reactions

Adverse reactions are uncommon and not severe. Immediate wheal and flare reactions occur occasionally and localized erythema may persist for 1 to 2 days. Immune tolerance has not been observed in infants born to women immunized during pregnancy. However, the safety of these vaccines in pregnant women has not been established.

Mumps Vaccine

Mumps is an acute infectious disease caused by a paramyxovirus. Subclinical infection is common. It has not been a reportable disease in all jurisdictions in Canada and the national incidence is unknown.

While complications are relatively frequent, permanent sequelae are rare. Ten to 12% of all cases of aseptic meningitis are caused by mumps virus. Deafness, which is usually transient but occasionally permanent, may follow damage of the auditory portion of the eighth cranial nerve. In adults, orchitis occurs in 15-25% of male cases and oophoritis in 5% of females. Involvement of the generative organs is frequently unilateral and sterility as a result of mumps is rare.

Preparations Used for Immunization

Mumps virus vaccine is a live attenuated virus vaccine and is supplied alone or in combination with measles and rubella vaccine (see Appendix). It is prepared from the Jeryl Lynn strain which is grown in chick embryo cell cultures. A single dose of this live vaccine produces an antibody response in over 95% of susceptible individuals. Reactions to the vaccine are rare and antibody levels, while lower than those that follow natural disease, persist for at least 15 years. Booster doses are not required.

Recommended Usage

Live attenuated mumps vaccine is recommended for all children 12 months of age or older who have had neither the vaccine nor the disease. The dosage and route of administration should be those indicated by the manufacturer. It may be given alone or in combination with measles vaccine or with measles and rubella vaccines, but should never take precedence over measles vaccination. These combined preparations may be used safely in persons already immune to any of the components. Mumps vaccine alone is of value for children approaching puberty or adults, especially males, who have had neither mumps nor mumps vaccine.

While mumps vaccine will probably not abort an established infection with mumps virus, there is no contraindication to administration of vaccine to contacts and this procedure can be used in attempts to limit the extent of an epidemic.

Adverse Reactions

There have been a few reports of parotitis and fever following vaccination. Mild short-lived skin rashes and pruritis have occasionally been reported.

A small number of hypersensitivity reactions to combined measles, mumps and rubella vaccine have been reported in persons who on eating eggs suffer anaphylactic hypersensitivity manifested by hives, swelling of the mouth and throat, difficulty in breathing, hypotension, and shock.

Contraindications

In common with other live vaccines, mumps vaccine should not be given to individuals whose immune mechanism is impaired as a result of disease, injury or therapy as detailed on page 11. As with other live vaccines, it should not be administered to pregnant women. Currently there are no data to indicate a link between diabetes and mumps vaccination.

Severe immediate allergic reactions to vaccines produced in chick embryo cell culture have been reported in a small number of children with anaphylactic hypersensitivity to eggs. Individuals with a history of anaphylactic

reactions to egg ingestion (hives, swelling of the mouth and throat, difficulty breathing, hypotension and shock) should not be given mumps vaccine. Persons who have egg allergies that are not manifested by anaphylactic symptoms and those with allergies to chickens or feathers may be vaccinated in the usual manner.

Since mumps vaccine contains trace amounts of neomycin, persons who have experienced anaphylactic reactions to topically or systemically administered neomycin should not receive mumps vaccine.

Pertussis Vaccine

Pertussis (whooping cough) is a highly communicable bacterial disease, caused by *Bordetella pertussis*, that has its greatest incidence of complications and its highest mortality in infants. Most deaths from pertussis occur in the first year of life. Since severity and fatality are greatest in infancy, protective measures such as immunization should be initiated as early in life as possible. Infants born to apparently immune mothers are highly susceptible to infection and there is no evidence of the infant's immune response being interfered with by maternal antibody when the vaccine is given to young infants.

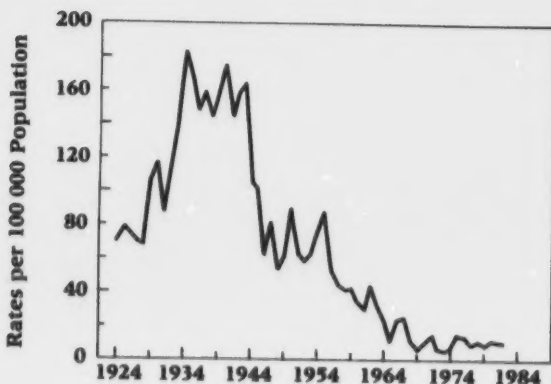
During the last 25 years, immunization has been widely practised and the incidence and mortality from pertussis in Canada have declined remarkably. In recent years approximately 2500 cases and about 3 deaths have been reported annually.

Preparations Used for Immunization

Pertussis vaccine is a suspension of killed *B. pertussis* organisms prepared from strains belonging to the commonly occurring serotypes. It may be prepared either as plain vaccine or in the adsorbed form, which contains an aluminum adjuvant. The potency of the adsorbed products is known to be greater than that of fluid vaccine.

Pertussis vaccine is usually given combined with other agents, either diphtheria and tetanus toxoids (DPT), or diphtheria and tetanus toxoids plus inactivated polio vaccine (DPT-Polio). It is also available as a single preparation (see Appendix). In combination vaccines, the pertussis

**Pertussis:
Reported Cases,
Canada, 1924-1982,
Rates per 100 000**



Pertussis vaccine introduced in 1943

component potentiates the antibody response to the polio, diphtheria and tetanus antigens.

Recommended Usage

Primary immunization consists of 4 doses of vaccine, usually given as a combined preparation, DPT or DPT-Polio, the first 3 doses being given at intervals of 4 to 8 weeks beginning at two months of age, and the fourth dose 1 year after the third. A single booster dose is given to children of 4 to 6 years.

The dosage and route of administration should be as recommended by the manufacturer. Adsorbed vaccines are given intramuscularly. It is important that pertussis

vaccination should begin by 2 months of age and be completed in accordance with the recommended schedule (see Part 2) to ensure the greatest possible protection to the young infant, in whom the disease can be very serious. Because the incidence and severity of the disease greatly decrease with age, and because adverse reactions are more common in older children and adults, pertussis immunization is not generally recommended for persons aged more than 6 years.

Protection from disease afforded by the vaccine decreases as the time interval since vaccination increases.

Infection in immunized persons may cause bronchitis without typical "whooping". Illnesses clinically indistinguishable from "whooping cough" can be caused by adenoviruses and other *Bordetella* species, and may lead to a false assumption of ineffectiveness of pertussis vaccine.

Adverse Reactions

Pertussis vaccine is usually administered in combination with diphtheria and tetanus toxoids; it is responsible for most of the reactions to DPT. Minor reactions such as transient local discomfort, induration and fever are seen in 50 to 75% of vaccine recipients but are self limited. Drowsiness and anorexia are also common. Persistent crying (3%) or screaming (0.1%) has also been reported in conjunction with pertussis vaccination. A hypotensive, hyporesponsive (shock or collapse) state has been reported to occur at a frequency of about 1:1 750 injections of DPT. Convulsions, usually accompanied by fever, have been reported at the same rate but complete recovery is usually seen. Encephalopathy has been estimated from a prospective British study to occur at a rate of one in 110 000 injections, with permanent sequelae resulting from one in 310 000 injections.

In comparisons of adverse effects occurring after diphtheria-pertussis-tetanus (DPT) vaccine with those following diphtheria-tetanus (DT) vaccine, minor local reactions have been reported in about 60% of DPT recipients compared with 10% of those given DT; fever was seen in 46% given DPT compared to 10% after DT; drowsiness in 31% with DPT compared to 15% with DT; and persistent crying in 3% given DPT but less than 1% of those given DT.

Contraindications

Pertussis vaccine should not be given to children who a) have had high fever (more than 40.5°C), convulsions, screaming episodes, shock, symptoms of encephalopathy, or thrombocytopenia following a previous dose of pertussis vaccine; b) are suffering from an evolving neurological disorder.

In infants and young children who have a history of seizures before receiving DPT vaccine or who develop seizures before the primary series is completed, initiation or continuation of pertussis immunization should be deferred until an evolving neurological disorder can be excluded. For infants and young children with stable neurological conditions, including well controlled seizures, the benefits of pertussis immunization generally outweigh the risks, since such infants may be at increased risk of complications if they contract pertussis.

When pertussis immunization is contraindicated or deferred, immunization with diphtheria and tetanus toxoids, when needed, can be continued using combined diphtheria-tetanus toxoid (DT) without pertussis. A plain pertussis vaccine is available for administration to infants whose pertussis immunization was deferred.

Pertussis-containing vaccine is not recommended routinely for persons over the age of 6 years.

Plague Vaccine

Plague is an acute disease caused by the bacillus *Yersinia pestis* transmitted from the natural reservoir in wild rodents and their ectoparasites. The fatality rate in untreated cases is about 50% in bubonic plague, while septicemic and pneumonic plague are usually fatal. Plague occurs in various parts of Asia, Africa and South America and also in the western third of the United States where a few human cases occur each year following exposure to infected wild rodents or their fleas. It occurs less commonly after exposure to other wild animals and rarely after exposure to infected dogs and cats. Cases of human plague have not been reported in Canada for more than 50 years.

Preparations Used for Immunization

Plague vaccine is a formalin-killed, phenol-preserved suspension of *Y. pestis*. The effectiveness of plague vaccines has never been measured precisely; field experience suggests that vaccination reduces the incidence and severity of disease resulting from the bite of infected fleas, but the degree of protection against primary pneumonic plague is unknown. (Thus persons exposed to pneumonic infection should receive anti-microbial prophylaxis regardless of their vaccination history).

Recommended Usage

Selective vaccination is recommended for

- a) persons who have frequent and regular contact with wild rodents in any area where plague is enzootic;
- b) laboratory personnel who work with *Y. pestis* or plague-infected rodents.

Routine vaccination is not indicated for persons living in plague enzootic areas or for most travellers to countries that are reporting cases.

Vaccine should be administered intramuscularly according to the manufacturer's directions. A primary series consists of two doses four weeks apart, and a third dose three to six months later. For persons remaining at risk, three booster doses should be given at six monthly intervals; thereafter boosters are given every one to two years.

Adverse Reactions

Primary immunization may result in general malaise, headache, fever, mild lymphadenopathy and redness and swelling at the injection site. These reactions occur more often with repeated injections.

Contraindications

Plague vaccine should not be given to persons who have had serious local or systemic reactions to previous doses. It is not recommended during pregnancy unless there is a substantial risk of infection.

Pneumococcal Vaccine

A vaccine is available against disease caused by 23 commonly occurring types of *Streptococcus pneumoniae* (pneumococcus).

The incidence of morbidity from pneumococcal infection in Canada is unknown; it is not a notifiable disease. About 7000 patients with pneumococcal pneumonia are treated annually in hospitals, about half being over 45 years of age. Approximately 200 deaths are attributed annually to pneumococcal pneumonia.

The great majority of strains of pneumococcus are highly susceptible to penicillin and other antibiotics; however, low level resistance to penicillin has been detected in about 2% of strains in Canada.

Preparations Used for Immunization

Pneumococcal Vaccine (Polyvalent) contains 25 μ g of capsular polysaccharide from each of 23 types of pneumococci (types 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F and 33F, Danish nomenclature). An earlier vaccine contained 50 μ g of each of 14 types. The present 23 types were chosen because of the frequency with which they have caused bacteremic and meningitic infection in the United States, Canada, and elsewhere in the world, and with due regard to cross-reactivity between types. The vaccine should be used in an identical manner to the earlier vaccine.

A single dose of vaccine given to healthy young adults stimulates a humoral antibody response to each of the component capsular polysaccharides. In children under 2 years of age, the antibody responses are poor and irregular. The protective titre of antibody against each type is not known.

The immunity conferred is type-specific but protection may also be given against some types that are closely related to but not identical with those represented in the vaccine (e.g. there are antigenic cross reactions between types 6A and 6B). The duration of immunity is unknown but antibody persists for at least five years. In healthy young adults in certain populations, vaccination has reduced the incidence of bacteremic pneumococcal pneumonia by more

than 80%. Recent studies indicate vaccine efficacy in the elderly and in chronically ill persons of approximately 70%. Vaccine efficacy may vary widely in patients with renal failure, sickle cell anemia or those with impaired immune responsiveness.

Recommended Usage

Pneumococcal vaccination should be of benefit to persons over the age of 2 years at the highest risk of developing severe pneumococcal infections; these include those with asplenia, splenic dysfunction or sickle-cell disease. The degree of efficacy of vaccine in these conditions is still uncertain, however, and vaccine failures may occur.

Other persons considered to be at increased risk from pneumococcal disease and who should benefit from vaccine include those with hepatic cirrhosis, chronic cardiorespiratory disease, chronic alcoholism, chronic renal disease, Hodgkin's Disease, and conditions associated with immunosuppression. Since mortality from bacteremic pneumococcal disease increases with advancing age, particularly over 60 years, the age of the patient is an additional factor to consider.

It is likely that vaccine will be of value in institutions for the elderly chronically ill, particularly in a closed population with a high rate of endemic disease, and for patients who have recently received hospital care since they have been shown to be at increased risk of serious pneumococcal disease.

Adverse Reactions

No serious reactions to a single dose of vaccine have been reported. Local soreness and erythema are quite common. Occasionally slight fever may occur.

Following second and subsequent doses of pneumococcal vaccine in adults, local reactions of the Arthus type can be very severe and systemic reactions such as high fever may occur.

Contraindications

Adults should not be given more than one dose of pneumococcal vaccine. Vaccine should not be given during febrile illness. Persons who received the 14-valent vaccine should not be given the 23-valent vaccine.

Vaccination of pregnant women should not be performed unless there is considered to be a substantial risk of pneumococcal disease.

Vaccination of children under 2 years of age is not recommended because it is relatively ineffective.

Poliomyelitis Vaccines

Poliomyelitis is caused by infection with one of three antigenic types of poliovirus. The last major epidemic occurred in 1959 when 1887 paralytic cases occurred. Following the introduction of inactivated poliovirus vaccines (IPV) in Canada in 1955 and of trivalent oral poliovirus vaccine (OPV) in 1962, the indigenous disease has virtually been eliminated. In the 1970s an average of only 3 cases was reported each year. Nine cases occurred in 1978 among unimmunized contacts of imported cases. All had rejected vaccination on religious grounds. Spread to the general population did not occur.

The circulation of "wild" polioviruses in the Canadian population has decreased in recent years, and it is unlikely that inapparent infections with these strains now contribute significantly to maintaining immunity. The maintenance of the highest possible level of vaccine-induced immunity in the population by systematic immunization programs for infants and children is therefore clearly essential.

Preparations Used for Immunization

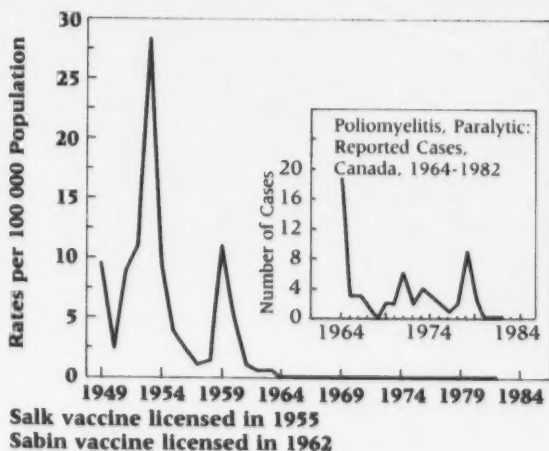
Two types of poliovirus vaccine are licensed for use in Canada:

1) *Inactivated Poliomyelitis Vaccine (IPV)*

The vaccine contains poliovirus types 1, 2 and 3 propagated in cultures of monkey kidney epithelial cells and subsequently inactivated with formalin. IPV is also available combined with diphtheria, pertussis and tetanus vaccines.

The vaccine is inoculated subcutaneously using the dose specified in the manufacturer's package insert. When used as recommended, IPV produces immunity to all 3 polioviruses and induces a persistent state of immunologic responsiveness. IPV induces little or no locally protective

Poliomyelitis, Paralytic: Reported Cases, Canada, 1949-1982



antibody in pharyngeal and intestinal secretions. Live polioviruses, either "wild" or vaccine strains, may still infect individuals immunized with IPV. Although individuals may excrete the virus in the feces, there is epidemiological evidence that circulation of "wild" polioviruses is greatly reduced in communities where only IPV has been used.

Primary vaccination with 4 subcutaneous doses of the currently available IPV (the first three at intervals of 1 to 2 months and the fourth 6 to 12 months later) confers immunity to all 3 types in more than 95% of recipients.

2) *Live, Oral Poliovirus Vaccine (OPV)*

This vaccine contains attenuated strains of poliovirus types 1, 2 and 3 propagated in cultures of monkey kidney epithelial cells.

The immune response to OPV is similar to that induced by natural infection with poliovirus and includes the development of secretory antibody within the intestinal tract. This is believed to prevent subsequent infection with "wild" polioviruses and their dissemination by the fecal-oral route to susceptible individuals in the community. OPV also interferes with simultaneous infection with "wild" polioviruses and is thus of particular value in the control of epidemics.

Fecal excretion of vaccine strains of poliovirus, which occurs following administration of OPV, may lead to infection of close contacts. This indirect immunization of persons other than primary vaccine recipients is regarded as largely beneficial since it results in protection of more individuals than the number actually vaccinated, but in a very small number of infected contacts, especially adults, paralytic disease may occur.

A primary course of 3 doses of OPV, the first 2 being given at least 5 weeks apart and the third given 8 to 12 months after the second will give long-lasting immunity to all 3 types in more than 95% of recipients.

Recommended Usage

Infants and Children

Immunization against poliomyelitis may be undertaken with IPV or OPV. Both have successfully controlled poliomyelitis in various parts of Canada. The recommended schedules presented in Part 2 apply to either vaccine. Breast feeding is not a contraindication to giving OPV to an infant. Some authorities recommend the administration of a 3-dose course of IPV prior to giving OPV. This still allows development of the immune response characteristic of OPV, including intestinal secretory antibody, and fecal excretion of OPV occurs.

Children who move to a jurisdiction where a different type of polio vaccine is used from the one they have previously been given may continue their immunization with the other vaccine and there is no need to restart the series.

Adults

Public health programs for the routine immunization against poliomyelitis of adults living in Canada are not considered necessary. Most adults are already immune and have a very low risk of exposure to polioviruses in North America.

Immunization with poliomyelitis vaccine is recommended, however, for **certain categories of adults** who are at greater risk of exposure to poliovirus than the general population. Such persons include:

- a) travellers to areas or countries where poliomyelitis is epidemic or endemic;
- b) laboratory workers handling specimens which may contain polioviruses;
- c) health care workers in close contact with patients who may be excreting polioviruses;
- d) unvaccinated parents of infants who are to be given OPV;
- e) residents of communities where routine immunization of infants and children has not been practised.

In the case of the above categories the following recommendations apply:

A. For unvaccinated adults, primary immunization with IPV is recommended whenever this is feasible. IPV is chosen because the risk of vaccine-associated paralysis following OPV is slightly higher in adults than in children. Three doses are given at intervals of 1 to 2 months and a fourth is given 6 to 12 months after the third.

The following special recommendations are made for circumstances where time will not allow at least 3 doses of IPV to be given before protection is required:

(1) Travellers who will depart in less than 2 months but who have 4 or more weeks available should be given 2 doses of IPV at least 4 weeks apart. When less than 4 weeks remain before travel, a single dose of OPV is recommended. In both instances the remaining doses of vaccine should be given later at the recommended intervals.

(2) Unvaccinated parents or other adult household contacts of infants who are to be given OPV carry a very

small risk of developing OPV-associated paralysis. It will generally not be practical for such persons to be protected with IPV before the infant is immunized, and the very small risk may most feasibly be reduced by giving them OPV at the same time as the first dose is given to the infant. Vaccination of infants, however, should not be delayed by this procedure. Arrangements should be made for the adults to complete their basic course of immunization.

B. Incompletely Immunized Adults, who have previously received less than a full primary course of IPV or OPV should be given the remaining required doses, preferably of the same vaccine, regardless of the interval since the last dose.

C. Adults Previously Given a Complete Primary Course of OPV or IPV, may be given a single dose of IPV or OPV if more than 10 years have elapsed since their last dose of vaccine. The need for this or other additional doses of poliovirus vaccine has not been established.

Outbreak Control

If a case of paralytic poliomyelitis caused by "wild" virus appears in a community, OPV should be administered to all individuals over 6 weeks of age who have not been completely immunized or whose immunization status is uncertain.

IPV is not recommended for the control of outbreaks of poliomyelitis.

Adverse Reactions

In rare instances OPV has been associated temporally with paralytic disease in vaccine recipients or their close contacts. Between 1962 and 1982, vaccine-associated paralysis in Canadian recipients of OPV occurred at the rate of 1 case per 4.8 million doses of vaccine distributed, and in contacts of vaccinees, 1 case per 3.7 million doses distributed.

The effectiveness of OPV in preventing and controlling paralytic poliomyelitis is so great that the extremely small risk of vaccine-associated paralysis is not a contraindication to its widespread use in routine immunization programs for infants and children.

Side effects of currently available IPV are limited to minor local reactions.

Contraindications

Administration of OPV is contraindicated in the presence of acute severe illness and in all cases of leukemia, lymphoma, generalized malignancy, or advanced debilitated states. OPV must never be given to patients who are immunodeficient or on immunosuppressive therapy, nor to persons who will have household or similar close contact with such patients in the following 4 weeks. These patients and their contacts may be given IPV without risk, but the protection afforded to immunocompromised persons may be limited.

Pregnancy is neither an indication for vaccination against poliomyelitis nor a contraindication when protection is urgently indicated, such as during an epidemic. Although there is no evidence to suggest that a pregnant woman or her fetus is at greater risk from OPV than are other persons, when primary immunization is necessary it should be undertaken with IPV except during control of an outbreak.

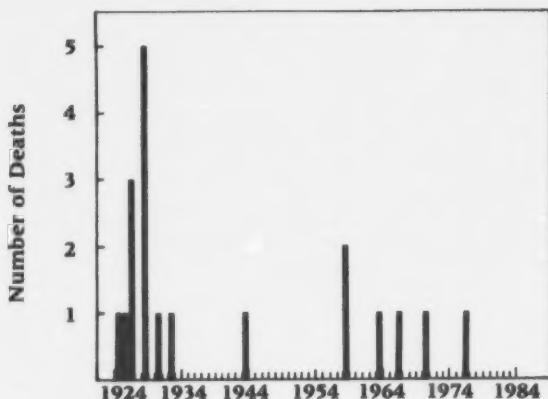
Rabies Vaccine

Introduction

Rabies virus can infect any mammal. It is detectable mainly in wildlife species and in the domestic livestock and pets they attack. In recent years, most reported wildlife infections in British Columbia have been in bats; in Alberta, Saskatchewan and Manitoba in skunks; and in Ontario and Quebec in foxes and skunks. Wildlife rabies was not reported in any of the Atlantic provinces in 1981 or 1982. Domestic dogs and cats account for less than 10% of animal rabies reported but bites of these species account for a much larger percentage of courses of antirabies post-exposure treatments given to humans.

Since reporting began in 1925, 19 persons have died of rabies in Canada. A decision on the management of a person who has been exposed to the risk of rabies infection must be made rapidly and judiciously since delay in starting a course of vaccine reduces its effectiveness, and the disease

**Rabies:
Number of Deaths
Canada, 1924-1982**



once established is almost always fatal. Close to 3000 persons in Canada received post-exposure treatment in 1982 because of exposure to rabid or possibly rabid animals.

Preparations Used for Immunization

Human Diploid Cell Vaccine (HDCV), which became available in 1980, is now the preferred rabies vaccine for both pre-exposure and post-exposure use because of its greater antigenicity and the lower incidence of adverse reactions compared to previously used vaccines.

In the past, Rabies Vaccine (Tissue Culture Origin) and Rabies Vaccine (Duck Embryo) (DEV) were used for pre-exposure prophylaxis, and DEV and Rabies Vaccine (Semple Type) for post-exposure management. DEV is no longer manufactured but the other vaccines may still be available in limited quantities.

HDCV is prepared from rabies virus grown in WI-38 or MRC-5 human diploid cell culture and inactivated with beta-propiolactone. There has only been one reported treatment failure among several hundred people exposed to known rabid animals (and vaccine alone rather than the recommended combination of vaccine and immune globulin was used in this case).

Recommended Usage

Post-Exposure Management

Rabies prophylaxis must be considered in every incident of animal bite unless rabies is known to be absent from the animal population. The following factors should be taken into consideration:

1. **Species of Animal:** Among the animals in Canada most often infected with rabies are foxes, skunks, cattle, dogs, cats, and bats. Human exposures to livestock are usually confined to salivary contamination, with the exception of horses and swine in which biting incidents have been reported. Risk of infection following exposure to rabid cattle is low, but over 30 cases of human disease following such exposure are reported in the world literature. **Squirrels, hamsters, guinea-pigs, gerbils, chipmunks, rats, mice, other rodents or rabbits and hares are rarely found to be infected with rabies and are not known to cause human rabies in Canada and the United States; their bites seldom, if ever, call for rabies prophylaxis.** Information regarding the prevalence of rabies in various animal populations in a province can be obtained from the Medical Officer of Health or a government veterinarian. The only known cases of human-to-human transmission of rabies were patients who received corneal transplants from persons who had died of unrecognized rabies. Tissues from persons who die of encephalitis of unknown etiology should not be used as donor transplants.
2. **Biting Incident:** Each incident requires full investigation. The behaviour of the animal may be significant. An unprovoked attack is more apt to indicate that the an-

imal is rabid. Conversely, a rabid animal may become uncharacteristically quiet. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as **provoked**.

3. **Type of Exposure:** A significant exposure is considered to be (a) any bite or (b) contamination of scratches, abrasions, open wounds or mucous membranes with saliva, body fluids or tissue from a rabid animal.
4. **Vaccination Status of Biting Animal:** A dog or cat known to have been fully immunized against rabies in Canada is unlikely either to develop or transmit rabies. Caution should be exercised in evaluating the significance of rabies vaccination given to an animal in another country.

Management of Animals Involved in Biting Incidents

Any animal identified as having bitten a human and suspected of being rabid should be reported to the local Medical Officer of Health and to the nearest District Office of the Food Protection and Inspection Branch, Agriculture Canada. District Veterinarians are familiar with the federal regulations concerning rabies and, if necessary, will collect and ship appropriate specimens to a federal laboratory for diagnosis (**see Footnote**). Stray or unwanted dogs or cats

Footnote: Further information and advice is readily obtainable from Food Protection and Inspection Branch Regional Offices at 1222 Main Street, Moncton, N.B., E1C 8L4, telephone (506) 388-7400; 685 Cathcart Street, Montreal, P.Q., H3B 1M7, telephone (514) 283-5663; 4900 Yonge Street, Suite 1210, Toronto, Ontario, M2N 6G7, telephone (416) 226-9262; 269 Main Street, Winnipeg, Manitoba, R3C 1B2, telephone (204) 949-2200; 1975 Scarth Street, Regina, Sask., S4P 2H3, telephone (306) 359-5210; 574-220-4th Avenue, S.E., Calgary, Alberta, T2P 3L2, telephone (403) 231-4687; 1001 West Pender Street, Vancouver, B.C., V6E 2M7, telephone (604) 666-1575.

and other biting animals, *particularly wild animals*, should be humanely killed immediately in such a manner as to do as little damage as possible to the head, which should be submitted for laboratory examination. A domestic dog or cat that is clinically normal may instead be confined, but if this is done it **must** be kept under observation for 10 days regardless of whether the animal has a history of vaccination. If the animal is still clinically well after that time, a diagnosis of rabies is highly unlikely. If it becomes ill during the holding period it should be killed and the head submitted for examination.

Management of Persons Following Possible Exposure to Rabies

The following recommendations are intended as a guide and may need to be modified in accordance with the specific circumstances of the exposure to rabies.

- A. Local Treatment of Wounds: **Immediate washing and flushing with soap and water, detergent, or water alone is imperative and is probably the most effective procedure in the prevention of rabies.** This should be followed by application of either 70% alcohol, tincture or aqueous solutions of iodine or 0.1% quaternary ammonium compound (first removing all traces of soap, which neutralizes the activity of the latter compound). Suturing the wound should be avoided if possible. Tetanus prophylaxis and antibacterial drugs should be given as required.
- B. Immunizing Agents: There are two types of immunizing products: (1) **Vaccines**, which contain inactivated virus and induce an active immune response beginning in 7 to 10 days and persisting for at least a year; (2) **Rabies immune globulin (RIG)**, which provides rapid protection that persists for only a short period of time (half-life about 21 days).

Vaccine and immune globulin should be used concurrently for optimum post-exposure prophylaxis against rabies, except in certain previously immunized persons, as indicated below:

Vaccines: *Post-exposure prophylaxis should be started as soon as possible after exposure and should be offered to exposed*

persons regardless of the elapsed interval. Prophylaxis may be started as late as 6 or more months after exposure. Human Diploid Cell Vaccine (HDCV) is the vaccine of choice and should be administered in conjunction with RIG. The route of administration should be that recommended in the manufacturer's package insert.

Five doses of HDCV should be given: the first dose (on day 0) as soon as possible after exposure, and additional doses on each of days 3, 7, 14, and 28 after the first dose. A single dose of RIG should also be given on day 0 as described below. Previous recommendations required an antibody determination 2 to 3 weeks after the fifth dose, but experience has shown this to be unnecessary.

Indication for Discontinuation of Post-exposure Prophylaxis: A course of vaccine may be discontinued if fluorescent antibody tests of an animal killed at the time of attack prove to be negative.

Rabies Immune Globulin: A dose of 20 I.U./kg of RIG should be administered on one occasion, as soon as possible after exposure. Up to one half the dose should be infiltrated around the wound if practical; the remainder should be given intramuscularly using a separate syringe and needle. Because of interference with active antibody production, *the recommended dose should not be exceeded.* Since vaccine-induced antibody begins to appear within one week, there is no value in administering RIG more than 8 days after initiating a vaccine course.

Under no circumstances should vaccine be administered in the same syringe or at the same site as RIG.

Post-exposure Therapy of Previously Immunized Persons: When a person exposed to rabies has previously been vaccinated with HDCV (either a pre-exposure or post-exposure course) *or* has had previously demonstrated rabies antibody, only 2 further doses of HDCV, one immediately and another three days later need be given. **RIG should not be given in these cases.**

If vaccine other than HDCV had been used for previous immunization and seroconversion has not been demonstrated, full post-exposure rabies prophylaxis with HDCV including rabies immune globulin should be started. A

serum sample may be collected before vaccine is given and if adequate antibody is demonstrated, the course can be discontinued provided the 2 doses of vaccine indicated above have been given.

Post-Exposure Rabies Prophylaxis Guide

Details of Animal	Nature of Exposure	Management of Exposed Person
a) Rabid b) Suspect Rabid c) Wild animal ¹ in endemic area, particularly skunk, fox, coyote, raccoon, bat d) Escaped dog or cat in endemic area (unless exposure was clearly provoked)	No skin or mucosal contact with animal or casual contact, e.g. petting with no possible contamination of broken skin or a mucous membrane	No treatment
	Bite; or contamination of scratch, abrasion, open wound or mucous membrane with saliva, body fluids or tissue	1. Local treatment of wound 2. RIG (local and intramuscular) 3. Full course ² of HDCV
Apparently healthy domestic dog or cat that can be held under observation for 10 days	Bite; or contamination of scratch, abrasion, open wound or mucous membrane with saliva, body fluids or tissue	1. Local treatment of wound 2. At first sign of rabies in the animal during holding period give RIG (local and intramuscular) and start full course of HDCV

Abbreviations: RIG – Rabies Immune Globulin (Human).

HDCV – Human Diploid Cell Vaccine.

NOTES:

1. (a) If available, the animal should be killed and tested as soon as possible; holding for observation is not recommended.

(b) Bites of squirrels, chipmunks, rats, mice, other rodents, rabbits, and hares are seldom, if ever, an indication for rabies prophylaxis.

2. Vaccine may be discontinued if fluorescent antibody tests of animal killed at time of attack are negative.

Pre-exposure Vaccination

Pre-exposure rabies vaccination is an elective procedure and should be offered to persons at potentially high risk of contact with rabid animals, e.g. veterinarians, animal handlers, certain laboratory workers, spelunkers, forest rangers, conservation officers, wildlife biologists, and certain travellers at high risk.

Three doses of HDCV are required, one on days 0, 7 and 21. The vaccine may be given as a 1.0 ml dose intramuscularly, or a 0.1 ml dose intradermally. Although the latter is associated with more local reactions, it is of comparable efficacy. Post-vaccination rabies antibody determinations are not normally required. If intradermal administration is chosen, the reconstituted vaccine should be used within 24 hours or discarded.

Booster Doses of Vaccine: A protective antibody titre is considered to be 1:16 by the rapid fluorescent-focus inhibition test. Persons with continuing high risk of exposure such as certain veterinarians should have their serum tested every 2 years; others working with live rabies virus in laboratories or vaccine-production facilities and who are at risk of inapparent exposure should be tested every 6 months. Those with inadequate titres should be given a booster dose of HDCV. Persons previously immunized with other vaccines should be given sufficient doses of HDCV to produce an adequate antibody response.

Rabies vaccine of tissue culture origin produced in hamster kidney cells (HKV) may be used for pre-exposure immunization if HDCV is not available. Four doses, the first three at one month intervals and the fourth 3 to 6 months later, are required. Since up to 20% of individuals do not respond to this course, post-vaccination antibody determinations are required and additional doses should be given to those who fail to respond.

Adverse Reactions

HDCV: Local reactions such as pain, erythema, swelling or itching at the injection site may occur in about 25% of recipients; mild systemic reactions such as headache, nausea, abdominal pain, muscle aches, and dizziness may

occur in about 20%. Systemic allergic reactions to HDCV characterized by generalized urticaria accompanied in some cases by arthralgia, angioedema, fever, nausea, vomiting, and malaise have been reported. These reactions have occurred in up to 7% of persons given a booster dose, with onset 2 to 21 days later, but were much less common in persons receiving primary immunization. Immediate anaphylactic reactions have occurred in 1 in 10,000 persons given HDCV.

HKV: Local and systemic reactions are not common with HKV and neuromuscular reactions have not been reported.

RIG: Local pain and low grade fever may follow administration of RIG.

Precautions and Contraindications

A history of any previous hypersensitivity reaction to HDCV should be elicited. Hypersensitive individuals should be vaccinated only under strict medical supervision.

There is no contraindication to the use of rabies vaccine following significant exposure to a proven rabid animal.

Corticosteroids and immunosuppressive agents may interfere with the development of active immunity and predispose the patient to developing rabies. If rabies post-exposure prophylaxis is given to persons receiving steroids or immunosuppressive therapy, it is important that serum should be tested for rabies antibody to ensure that an adequate response has developed.

Pregnancy is not a contraindication to post-exposure prophylaxis, but it would be prudent to delay pre-exposure vaccination of pregnant women unless there is a substantial risk of exposure.

Rubella Vaccine

Rubella is a common viral disease of childhood which is difficult to diagnose clinically except during epidemics.

The major objective of vaccination is the prevention of rubella infection in pregnancy in order to prevent the congenital rubella syndrome (CRS). This syndrome may in-

clude congenital heart disease, cataracts, deafness, and mental retardation which may not become manifest for several years. The frequency of fetal damage following maternal infection in the first trimester of pregnancy is estimated to exceed 20%. Infected infants who appear normal at birth may later show eye, ear or brain damage. Congenital infection may become chronic and give rise to such problems as diabetes mellitus and panencephalitis later in life.

Rubella has been a notifiable disease in Canada since 1924, with the exception of the period 1959 to 1968. The disease has occurred in irregular 3 to 10-year epidemic cycles. At present, 86% of reported cases in Canada are under the age of 15 years.

Preparations Used for Immunization

Rubella Virus Vaccine currently licensed in Canada is a live attenuated virus, strain RA 27/3, prepared in human diploid cell culture. The vaccine is administered as a single subcutaneous injection. It stimulates the formation of antibodies to rubella virus in approximately 95% of susceptible individuals. Titres are generally lower than those observed in response to natural rubella infection, and antibody levels developed in response to earlier rubella vaccines have declined during a 10-year period of observation of children; however, this decline may not have great significance since any detectable level of antibody generally protects against viremic infection. Long-term protection is expected from vaccination; its duration is not yet known but studies indicate that it exceeds 10 years. Booster doses are not considered necessary.

Small quantities of virus may be detected in the nasopharynx of some vaccinees 7 to 28 days after vaccination, but transmission to contacts has not been documented. Therefore vaccine can safely be administered to persons in contact with susceptible pregnant women or immunocompromised persons. Asymptomatic reinfection, producing a rise in antibodies, has been observed in vaccinees with very low antibody titres. The significance of such reinfection is not entirely certain, but there is believed

to be no risk to susceptible contacts and it is very unlikely that immune women reinfected while pregnant would transmit virus to their fetuses.

Rubella vaccine is supplied singly or in various combinations with measles and mumps vaccines.

Recommended Usage

Infants and Children: Rubella vaccine should be given routinely to all children of both sexes at 12 months of age or as soon thereafter as possible, preferably in combination with measles and mumps vaccines. Children up to age 12 years who have no documentary evidence of having received vaccine should also be vaccinated. A clinical history of rubella is not a reliable indicator of immunity.

Adolescents and Adults: **Rubella vaccine should be given to all female adolescents and women of childbearing age** unless they have either laboratory evidence of detectable antibody or documentary evidence of having received vaccine. Susceptibility should be determined by serological testing whenever possible. However, testing need not be undertaken where laboratory facilities are not readily available, where large numbers of adolescents or adult women are to be immunized, or where testing is likely to interfere with acceptance of delivery of the vaccine. There are no known adverse effects following administration of vaccine to immune women.

Administration of vaccine to pregnant women should be avoided. Inquiry regarding pregnancy should be made prior to vaccination. Women of childbearing age should be advised to avoid pregnancy for 3 months following vaccination.

In educational institutions such as schools, colleges, and universities, particular emphasis should be placed on protection of susceptible female staff and female students of childbearing age because of their relatively high risk of exposure.

In health care settings, the rubella immunity status of female employees of childbearing age should be carefully reviewed and those without documented immunity should be vaccinated unless there are contraindications. In addi-

tion, vaccine should be given to persons of either sex who may, through frequent face-to-face contact, expose pregnant patients to rubella.

Serological testing for rubella antibody should be a routine procedure during pre-natal care. Since up to one-third of cases of CRS occur in second and subsequent pregnancies, it is particularly important that all women found to be susceptible during pregnancy should receive rubella vaccine in the immediate post-partum period. Breast feeding is not a contraindication to rubella vaccination. Although vaccine virus has been detected in breast milk, no recognizable illness has been noted in infants fed by recently vaccinated mothers. Where immune serum globulin has been administered or a blood transfusion given, rubella vaccination should be delayed for 3 months. However, previous or simultaneous administration of anti-Rho (D) immune globulin has been shown not to interfere with the antibody response to rubella vaccination.

Laboratory tests for seroconversion after vaccination are unnecessary. If a serological test is done for some other reason and found to be negative despite a history of rubella vaccination, a repeat dose of vaccine may be given on one occasion. It is not necessary to repeat vaccination more than once even if subsequent serological tests are also negative as such individuals usually have other evidence of rubella immunity.

Adverse Reactions

Serious adverse reactions are rare. Rash and lymphadenopathy occur occasionally in vaccinated children and more frequently in susceptible women. Transient arthritis or arthralgia may occur 7 to 21 days after vaccination; they are uncommon in children, but occur with increasing frequency and severity in post-pubertal females. There have been rare reports of chronic or recurrent arthritis. Paresthesia or pain in the extremities lasting 1 week to 3 months has been reported rarely.

Contraindications

Live rubella vaccine is contraindicated in women known or suspected to be pregnant.

Rubella vaccine is occasionally administered to women who are subsequently found to have been pregnant at the time. The number of such cases investigated is still small and more information is needed before the vaccine can be conclusively considered non-teratogenic. However, reassurance can be given that in cases to date when susceptible women have received vaccine and carried their pregnancy to term, no adverse effects have been detectable in their infants. Rubella vaccination of a woman who is pregnant or who becomes pregnant in the following 3 months is not necessarily a reason for abortion, and the individual circumstances should be considered by the physician.

In common with other live vaccines, rubella vaccine should not be administered to patients whose immune mechanism is impaired as a result of disease, injury or therapy, or to persons known to be hypersensitive to vaccine components such as antibiotics used in its preparation, as may be indicated in the manufacturer's package insert.

Since rubella vaccine is prepared in human diploid cell culture, it can be given safely to persons allergic to eggs.

Management of Outbreaks

During outbreaks, persons at risk who have not been vaccinated should be given vaccine promptly without prior serological testing. A history of rubella illness is not a reliable indicator of immunity.

Even though rubella immunization is not protective when given after exposure, it is not harmful and will protect the individual in future if the present exposure does not result in infection.

Surveillance

All suspected and confirmed cases of rubella and congenital rubella syndrome should be reported to the appropriate health authority.

Smallpox Vaccine

The World Health Organization published the Declaration of the Global Eradication of Smallpox in May 1980. There are now no longer any indications for the use of smallpox vaccine in the civilian population. Its availability is restricted, and is limited to the Armed Forces.

If a smallpox vaccination certificate is believed to be necessary, it is recommended that a document be provided which waives vaccination on medical grounds.

Staphylococcus Toxoid

Staphylococcus toxoid is a combined preparation of the alpha and beta toxoids of *Staphylococcus aureus*. Its efficacy has not been proven in controlled studies. The toxoid is used primarily for the treatment of localized and recurrent staphylococcal infections, especially those of the skin. The preparation is not principally used to prevent disease in otherwise healthy persons and therefore is not considered further here.

Tetanus Toxoid

Tetanus is an acute and often fatal disease caused by an extremely potent neurotoxin produced by *Clostridium tetani*. The organism is ubiquitous and its occurrence in nature cannot be controlled. Immunization is highly effective, provides long-lasting protection and is recommended for the whole population.

Currently about 20 persons are hospitalized with tetanus each year. Over the past 5 years, 7 deaths were recorded, 5 in persons over 60 years of age.

Preparations Used for Immunization

Tetanus toxoid is prepared by detoxification of tetanus toxin with formalin. The toxoid is available in the plain (unadsorbed) form or combined with aluminum salts, generally aluminum phosphate, in the adsorbed form. Adsorbed toxoid is the agent of choice for primary immunization, but both forms are acceptable for booster doses.

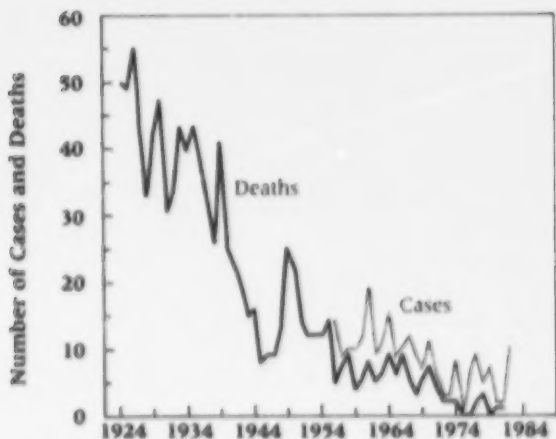
The toxoid is available alone or in various combinations with diphtheria toxoid, pertussis vaccine and inactivated poliomyelitis vaccine (for details see Appendix).

All preparations contain comparable amounts of tetanus toxoid.

Recommended Usage

Although tetanus toxoid may be used alone, the most commonly used preparation for primary immunization is a combination with diphtheria toxoid and pertussis vaccine

**Tetanus:
Number of Cases and Deaths,
Canada, 1924-1982**



Tetanus toxoid introduced in 1940

(DPT), sometimes with the addition of trivalent inactivated polio vaccine (DPT-Polio). The primary immunizing course of DPT or DPT-Polio in children consists of four doses. The time interval between the initial three doses should be 4 to 8 weeks; the fourth dose should be given one year after the third dose. The schedules recommended for childhood immunization and the timing of booster doses are shown in Part 2.

When tetanus toxoid is used alone, adsorbed toxoid is recommended in two doses given at least one month apart with a third dose 6 to 12 months later. In adults, consideration should be given to the use of the combined adult-type preparation of tetanus and diphtheria toxoid (Td). If fluid

toxoid is used, three doses are given at monthly intervals followed by a fourth 8 to 12 months later.

Booster doses are recommended at 10-year intervals. If given more frequently they may lead to severe local and systemic reactions.

Tetanus Prophylaxis in Wound Management

The following table summarizes the recommended use of immunizing agents in wound management. It is important to ascertain the number of doses of toxoid previously given and the interval since the last dose. When a tetanus booster dose is required, consideration should be given to choosing the combined preparation of tetanus and diphtheria toxoid formulated for adults (Td). Appropriate cleansing and debridement of wounds is imperative.

History of Tetanus Immunization (Doses)	Clean, Minor Wounds		All Other Wounds	
	Toxoid	TIG ¹	Toxoid	TIG ^{1,2}
Uncertain	YES	NO	YES	YES
0-1	YES	NO	YES	YES
2	YES	NO	YES	NO ³
3 or more	NO ³	NO	NO ⁴	NO

1. TIG - Tetanus Immune Globulin, Human.
2. Penicillin or a tetracycline may be given in addition.
3. Unless more than 10 years since last dose.
4. Unless more than 5 years since last dose.
5. Unless wound is more than 24 hours old.

Adverse Reactions

Adverse reactions to primary immunization with tetanus toxoid are rare. Following booster doses, local erythema and swelling are not uncommon and Arthus type sensitivity may occur. Severe local reactions are often associated with high levels of circulating antitoxin, which may be a result of doses of toxoid being given too frequently. Systemic reactions are uncommon. Generalized urticaria is the most frequent; anaphylaxis and peripheral neuropathy have also been reported.

Contraindications

Tetanus toxoid should not be given if a severe systemic reaction followed a previous dose. It is recommended that tetanus toxoid not be given to any patient who has received a booster dose in the preceding 5 years.

Persons who experience a major local reaction following a dose of tetanus toxoid should not be given another dose for at least 10 years. When a contraindication exists and a patient sustains a major or unclean wound, use of tetanus immune globulin should be considered.

Before giving a combined vaccine, particularly one containing pertussis vaccine, it is most important to ensure that there are no contraindications to the administration of any of the components.

Typhoid Vaccine

Typhoid fever is caused by *Salmonella typhi*, which differs from most other *Salmonella* species in that it rarely infects hosts other than man and frequently causes severe systemic illness in infected human beings. It is usually transmitted by food and drink that has been contaminated with excreta of a human case or carrier of *S. typhi*, and control of the disease is largely a matter of good sanitation and hygiene. The fatality rate ranges from 10% in untreated cases to less than 2% with appropriate antibiotic therapy.

The incidence of typhoid fever has declined steadily in Canada. Between 1977 and 1982, an average of 87 cases were reported annually. Many of these infections were contracted abroad but a small number occur in Canada, chiefly in areas where sanitation and hygiene are inadequate. Vaccine is believed not to have played a significant role in the decline in incidence of the disease.

Preparations Used for Immunization

Typhoid vaccine is a suspension of whole typhoid bacilli killed by heat and preserved by phenol. Although no vaccine can protect against an infection with a very large number of typhoid organisms, evidence from field trials suggests that acetone-dried vaccines, which are not yet available in Canada, may give up to 90% protection against

"ordinary" typhoid exposure; phenol-preserved vaccines are somewhat less effective.

Recommended Usage

Routine typhoid vaccination is not recommended but immunization with typhoid vaccine should be considered in the following situations:

- 1) intimate continuing exposure to a *S. typhi* carrier such as occurs in members of a household or institution in which a carrier lives;
- 2) travel to countries where typhoid fever is endemic. There is, however, generally no reason to use typhoid vaccine for persons in areas of natural disasters such as floods, or for persons attending rural summer camps;
- 3) laboratory workers who handle cultures of *S. typhi*.

Since typhoid vaccine does not confer complete protection against the disease, it is advisable that vaccinees be warned that immunization against typhoid is only one aspect of preventive measures against typhoid fever in an endemic country, or high risk situation, and that care in selection of food and water is of primary importance. They should also be reminded of the need for booster doses (see below).

Typhoid vaccine is not recommended for the control or containment of typhoid outbreaks in Canada.

TAB Vaccines: The effectiveness of paratyphoid A vaccine has never been proven, and field trials have shown that paratyphoid B vaccine is relatively ineffective. Use of combined typhoid- paratyphoid (TAB) vaccine is not recommended and they are no longer available in Canada.

Administration: The size and timing of doses and the route of administration depend upon the method of preparation of the vaccine, and the instructions of the manufacturer should be followed carefully.

Primary immunization consists of three injections given optimally at least 4 weeks apart. For continued protection, single booster doses should be given at least every three years if risk of exposure continues. If more than three years have elapsed since the last dose, one booster dose is sufficient; another primary series is unnecessary.

Adverse Reactions

Following typhoid vaccination, local redness, tenderness and swelling can be expected for a few days. In some individuals there may be malaise, headache and pyrexia, which rarely exceed 24 hours in duration. Severe systemic reactions are rare. Reactions are especially common in persons who have had repeated injections of typhoid vaccine.

Contraindications

Typhoid vaccine should not be given to children who have a history of febrile convulsions.

Yellow Fever Vaccine

Yellow fever is endemic in the tropical areas of Africa and Central and South America. The disease may occur in two epidemiologic forms — urban, and sylvatic or jungle. Both forms are caused by the same virus. Urban outbreaks occur as a result of transmission of the virus among urban residents by the mosquito *Aedes aegypti*. This mosquito is widely distributed throughout the tropics. Jungle yellow fever is a disease of monkeys in the forests of Central and South America and Africa which is transmitted to man by forest mosquitos, e.g. to forestry workers or oil company employees.

Control includes elimination of *Aedes aegypti* from urban areas, and immunization of forest workers and urban residents who are at risk of exposure. Unimmunized Canadians could acquire yellow fever when travelling abroad but are unlikely to transmit the disease on their return to Canada since the recognized mosquito vectors do not occur in this country.

Preparations Used for Immunization

Yellow fever vaccine is a live vaccine prepared in chick embryos from the attenuated 17D strain. The lyophilized preparation should be stored at the temperature specified by the manufacturer until it is reconstituted by the addition of the recommended diluent. Unused vaccine must be discarded one hour after reconstitution.

Recommended Usage

Persons 6 months of age or older travelling or living in areas where yellow fever infection exists should receive a single subcutaneous injection of reconstituted vaccine.

Yellow fever vaccine is a legal requirement for persons travelling from an endemic region to certain receptive areas (i.e. areas where the disease is not present but could become active if introduced because of the presence of the vector mosquito). Current information on the countries for which an International Certificate of Vaccination is required can be obtained from local health departments.

Vaccination is also recommended for laboratory personnel who work with virulent yellow fever virus.

For purposes of international travel, yellow fever vaccine is administered only at Yellow Fever Vaccination Centres approved by the World Health Organization, and the vaccination is recorded in an appropriately validated International Certificate of Vaccination. A list of such Centres in Canada can be obtained through provincial or local health departments.

Immunity following vaccination develops 10 days after vaccination and persists for more than 10 years. Revaccination every 10 years is required for purposes of international travel and is recommended for those at special risk, such as laboratory personnel.

When both cholera and yellow fever vaccines are required, they are preferably given 3 or more weeks apart to avoid mutual interference with antibody responses. No interference with protection has been demonstrated, however, and they may be given simultaneously when circumstances make it necessary.

Adverse Reactions

The few reactions to 17D yellow fever vaccine that occur are generally mild, but aseptic meningitis has been reported in infants following immunization and for this reason vaccination is not recommended for those under the age of 6 months. Five to 10 per cent of vaccinees have mild headache, myalgia, low grade fever, or other minor symptoms 5 to 10 days after vaccination.

Because yellow fever vaccine is prepared from chick embryos, it may induce reactions of varying degrees of severity in individuals hypersensitive to eggs. Allergy severe enough to preclude vaccination is very uncommon and is said to occur only in those who are actually unable to eat eggs.

Contraindications

Yellow fever vaccine should not be given to patients whose immune mechanisms are suppressed by disease or therapy as detailed on page 11 or to persons sufficiently hypersensitive to eggs that they are unable to eat them. Vaccine is contraindicated for persons hypersensitive to any antibiotics in the vaccine. It is not recommended for infants under 6 months of age.

It is prudent on theoretical grounds to avoid vaccinating pregnant women with live yellow fever vaccine unless the risk of exposure is considered to be high.

Part 4

Passive Immunizing Agents

Introduction

Protection against certain infections or a reduction in the severity of the illness can be achieved by administration of preformed antibodies derived from humans or animals. The preparations available are of two types: standard immune globulin (IG) of human origin often referred to as "Immune Serum Globulin or Gamma Globulin"; and special preparations of either human or animal sera containing high titres of specific antibodies to a particular microorganism or its toxin, such as tetanus immune globulin. Products of human origin are preferable to those of animal origin because of the high incidence of adverse reactions to animal sera, and the longer-lasting protection generally conferred by human globulins.

Passive immunization should be considered when vaccines for active immunization are not available, or in certain instances when they have not been used before exposure to the infective agent, as may be the case when an unimmunized patient sustains a wound that may be contaminated with tetanus bacilli. Passive immunization may also have a role in management of immunosuppressed persons unable to develop an immune response to a vaccine. The beneficial effects provided by passive immunizing agents are of relatively short duration, and the degree of protection may be incomplete.

In these guidelines, emphasis is on the prophylactic use of immune sera, and only brief reference is made to their use as therapeutic agents in established infections.

Immune Globulin (Human) (IG)

Immune globulin (IG) is a sterile concentrated solution containing 16.5% of the gamma globulin fraction (principally IgG antibody but with traces of IgA, IgM and other serum proteins) obtained from pooled human plasma of venous or placental origin. The method of preparation ensures that IG is free from hepatitis A and B viruses and

concentrates antibodies into a small volume which can be injected intramuscularly. Maximum plasma levels of IgG are reached about 2 days after injection and the half-life in the recipient's circulation is 20 to 25 days.

IG is stable for prolonged periods when stored at 2° to 8°C. It should be administered only by intramuscular injection unless otherwise specified by the manufacturer. Antibody content will vary with the population from which blood is collected and so may not be consistent from time to time or country to country.

Intravenous immune globulin (IGIV) is a preparation which contains 5% immune globulin in 10% maltose and is intended for intravenous use. It is primarily used for replacement therapy in selected congenital or acquired immunoglobulin deficiency states. Dosage should follow the manufacturer's package insert instructions.

Recommended Usage

Prophylactic use of IG has been shown to be effective in a limited number of clinical situations.

1. Measles (Rubeola)

IG can be given to prevent or modify measles in a susceptible person within 6 days of exposure. To prevent disease it should be given as soon as possible after exposure, preferably within 3 days. The recommended dose of IG is 0.25 mL/kg of body weight (maximum dose – 15 mL). IG should be considered for susceptible household contacts of measles patients, particularly contacts under 1 year of age for whom the risk of complications is highest. When clinical measles does not develop in a person given IG, live measles vaccine should be given about 3 months later, but in infant's vaccination should be postponed until the first birthday. **IG should not be used in an attempt to control measles outbreaks.**

The dosage of IG for patients who have underlying malignant disease or who are otherwise immunologically deficient should be 0.5 mL/kg with a maximum of 15 mL. Immunocompromised patients should not receive live measles vaccine.

2. Hepatitis A

IG will provide protection against hepatitis A when administered intramuscularly before exposure or during the incubation period. Its relative effectiveness depends upon both the time of administration after exposure and the dose given.

For post-exposure prophylaxis, IG should be given as soon as possible after known exposure. It is of greatest value when given early in the incubation period. It is of little or no value when given more than 2 weeks after exposure. The recommended dose is 0.02 mL/kg for:

- 1) all household contacts;
- 2) inmates and staff of institutions for the mentally retarded or prisons in which there is an outbreak;
- 3) all children and staff in day-care centres where a case has occurred and conditions are such as would facilitate hepatitis transmission.

Routine administration to hospital personnel or fellow-workers who are contacts of a case in offices or factories is not recommended. Use in schools for pupils or teachers in contact with a case is not indicated unless there is evidence that transmission is occurring in the school or classroom. In common-source outbreaks of hepatitis A, recognition of the source usually occurs too late to allow administration of IG sufficiently early to be of value.

Pre-exposure prophylaxis is recommended for certain travellers to areas of high prevalence (see page 101-102).

3. Rubella

IG given soon after exposure to rubella may modify or suppress symptoms but is not likely to prevent infection or viremia. Therefore the routine use of IG in women early in pregnancy who are exposed to rubella is not recommended although it may be considered when termination of pregnancy is not acceptable. A dose of 20 mL may be given intramuscularly within 48 hours of contact. Serum specimens should be examined for rubella antibody before and for several months after IG administration to determine whether infection occurred. The effectiveness of IG in the prevention of congenital rubella is questionable because there are insufficient data available.

Precautions and Contraindications Relating to Use of IG

Large doses should be divided and injected intramuscularly at two or more sites. Currently available preparations, with the exception of IGIV, must not be given intravenously because of the risk of severe anaphylactic reactions. Reactions at the site of injection include tenderness, erythema and stiffness of local muscles which may persist for several hours. Mild fever or malaise may occasionally occur.

Pregnancy is not a contraindication to use of IG or other immune globulins.

Specific Immune Globulins (Human and Animal)

Specific immune globulins are derived from the pooled sera of persons with antibody to the specific infectious agents or from animals, usually horses, hyperimmunized against such an organism. Because of the relatively high risk of serum sickness following the use of animal products, human immune globulin should be used whenever possible. **Before immune globulin of animal origin is injected, sensitivity testing should be carried out in accordance with the manufacturer's recommendations.**

1. Botulism Antitoxin (Equine)

Licensed preparations include a trivalent (Types A, B and E) and a monovalent (Type E) antitoxin. They are used prophylactically for persons suspected of having eaten food contaminated with botulinum toxin, and therapeutically in persons with established or suspected botulism. The dose and route of administration are indicated in the manufacturer's package insert.

2. Diphtheria Antitoxin (Equine)

This preparation is used for the prevention of diphtheria in unvaccinated persons exposed to infection or for treatment of the disease.

Prophylactic Use. Asymptomatic unimmunized household or intimate contacts of patients with diphtheria should be given diphtheria antitoxin in addition to antibiotic prophylaxis if they cannot be kept under daily sur-

veillance for 7 days for evidence of diphtheria. An intramuscular injection of 1000 international units is given.

Treatment. Antitoxin should be administered without awaiting bacteriological confirmation when there is clinical suspicion of diphtheria. Dosage is purely empiric. After completion of the tests recommended in the package insert to rule out the danger of anaphylactic reaction, a dose of 20 000 to 120 000 units, depending on the weight of the patient and severity and duration of symptoms, should be given. Intramuscular administration usually suffices, but intravenous administration may be necessary in some cases. If sensitivity tests are positive, desensitization must be undertaken according to the manufacturer's recommendations.

3. Gas Gangrene Antitoxin (Equine)

The value of gas gangrene antitoxins in treatment is not universally accepted and their use prophylactically is no longer advocated.

4. Hepatitis B Immune Globulin (HBIG)

HBIG is prepared from pooled human plasma from selected donors with a high level of antibody to hepatitis B surface antigen (anti-HBs). When HBIG is unavailable, normal immune globulin (IG) may be used in its place in the same dosage but may be less effective.

HBIG is recommended for prophylaxis against hepatitis B infection as follows:

A. Persons exposed percutaneously (e.g. by needlestick accident) or by mucosal exposure to blood that may harbour hepatitis B virus. The recommended usage depends upon knowledge of the source of the blood and whether it has been found to be positive for hepatitis B surface antigen (HBsAg). Those expected to be at repeated risk may receive the first dose of a course of hepatitis B vaccine concurrently with HBIG, in which case a second dose of HBIG is not necessary:

a) *source of blood known, HBsAg status positive* (estimated risk of clinical hepatitis B is 1:20). Administer HBIG (0.06 mL/kg) as soon as possible, preferably within 24 hours after exposure, and repeat one month later.

b) *source of blood known, HBsAg status unknown.* The blood source should be tested for HBsAg. If negative, immune globulin need not be given. If found positive, give HBIG as in a) above. When the test result is unavailable within 24 hours, proceed according to the table below:

Probability of Source Being HBsAg Positive	Action to be Taken
High (e.g. acute hepatitis)	Give HBIG immediately (0.06 mL/kg). If source is HBsAg positive, repeat dose in one month unless vaccine has been given.
Intermediate (e.g. patients from high endemic areas, patients with Downs Syndrome in institutions, male homosexuals, and users of illicit intravenous drugs).	Give IG immediately (0.06 mL/kg). If HBsAg test is positive, give HBIG immediately and one month later unless vaccine has been given.
Low (e.g. average hospital patient).	Options: give IG or do not treat, depending on circumstances.

c) *source of blood unknown, HBsAg status unknown.* Estimated risk of clinical hepatitis is 1:2000.

Options: Give IG, or do not treat, depending on circumstances.

B. Exposure of the newborn

Infants born to HBsAg-positive mothers regardless of their HBeAg or anti-HBe status are at risk of developing hepatitis B infection and subsequent long-term virus carriage with or without chronic liver disease. The risk is highest when the mother is HBe antigen positive and lower when the mother has antibody to HBe antigen (anti-HBe). Recent studies have shown that HBIG reduces the risk of such carriage in newborns if given immediately after birth.

HBIG in a dose of 0.5 mL should be given to all infants born of HBsAg positive mothers within the first few hours after birth, preferably within 12 hours. If not immediately available, it should be given as soon as it can be obtained but efficacy decreases sharply after 48 hours.

Three 10 µg doses of hepatitis B vaccine should also be given to the infant starting as soon as possible after birth. The first dose may be given at the same time as the HBIG

dose but at separate site. Additional doses of vaccine should be given one and six months after the first. If administration of the first dose is delayed until 3 months of age, a second dose of HBIG should be given at that time.

HBsAg testing should be performed on all infants prior to the third dose of vaccine and any infant found to be positive needs no further preventive therapy. Testing for HBsAg and anti-HBs is recommended at 12 to 15 months of age to monitor the final success or failure of prophylaxis.

Precautions to be taken and adverse reactions to be expected are those described in the section on Immune Globulin (page 89).

C. Sexual Contacts of Acute Cases of Hepatitis B

HBIG is a single dose of 0.06 mL/kg will provide significant protection to a person exposed to an acute case of hepatitis B. It should be given within 14 days of the last exposure. Persons having continuing sexual contact with a patient in whom HBsAg antigenemia persists for more than 3 months should be given a second dose of HBIG and a course of hepatitis B vaccine begun. IG may be used in place of HBIG when this is unavailable.

5. *Pertussis Immune Globulin (Human)*

This is of unproven value in the prevention and treatment of pertussis in infants and young children. Its use is not recommended.

6. *Rabies Immune Globulin (Human)*

Passive immunization with this product is undertaken as part of post-exposure prophylaxis against rabies (see page 69).

7. *Tetanus Immune Globulin (Human) (TIG)*

The use of TIG in the management of wounds is discussed in the section on Tetanus Toxoid on page 80. When used in the treatment of tetanus, TIG should be administered intramuscularly in an effort to neutralize tetanus toxin in body fluids. It has no effect on toxin already fixed to nerve tissue. A dose of 10 000 units is recommended; this may be divided into three equal portions and injected into different sites in the hope of assisting absorption into the blood.

Precautions to be taken and adverse reactions to be expected are those described in the section on Immune Globulin.

8. *Varicella-Zoster Immune Globulin (Human) (VZIG)*

VZIG is prepared from pooled human plasma from persons with high antibody titres to varicella-zoster virus.

Passive immunization with VZIG is indicated after exposure to varicella or zoster in patients in whom the risk of serious morbidity or mortality from varicella is substantially increased. The following contact with patients suffering from varicella or zoster is considered significant exposure: continuous household contact; playing indoors for more than an hour with a contagious child; or contact in hospital a) with a patient in the same room, or b) by prolonged face to face contact with an infectious staff member.

VZIG is recommended for the following categories of exposed persons who do not have a history of chickenpox:

A. Immunocompromised persons without a definite history of varicella. These include those with immune deficiency disorders or neoplastic diseases and recipients of immunosuppressive treatment. Recipients of bone marrow transplants should be regarded as susceptible regardless of a prior history of chickenpox in either recipient or donor.

B. Newborn infants of mothers who develop varicella shortly before or after delivery. VZIG is indicated for newborns of mothers who develop chickenpox during the 5 days prior to or within 48 hours of delivery.

C. Premature infants. Exposed infants of less than 28 weeks gestation should receive VZIG regardless of maternal history as they may not have acquired transplacental maternal antibody. VZIG is indicated for all exposed premature infants whose mothers are not known to have had varicella.

Usage: VZIG is of benefit if administered within 96 hours of the exposure. The value of later administration is unknown. Protection is believed to last for 3 to 4 weeks. Susceptibles who are re-exposed more than 3 weeks after a dose of VZIG should be given another dose.

The recommended dose is 125 units (1 vial) per 10 kg body weight to a maximum of 625 units, administered

intramuscularly. The most appropriate dosage for adults is uncertain. Doses greater than 625 units may be needed in immunocompromised adults. VZIG is available through Canadian Red Cross distribution centres.

It should be noted that administration of VZIG may prolong the incubation period of varicella for up to 28 days.

Precautions that should be taken and adverse reactions that may be expected are those described in the section on Immune Globulin.

Part 5

Immunization of Health Care Workers

Hospital employees, laboratory workers, and other health care personnel are at risk of exposure to communicable diseases because of their contact with patients or material from patients with infections, both diagnosed and undiagnosed. It is therefore most important that their basic immunization be maintained. In certain instances, depending on the nature of their employment, additional immunization may be indicated. Optimal usage of immunizing agents in hospital staff will not only safeguard the health of staff members but may, in some instances, also protect patients from becoming infected by hospital employees.

The immunization status of each worker should be assessed at the time of initial employment. A full immunization history should be elicited and efforts made to obtain documentary evidence of the doses received and dates of administration. Persons who cannot provide acceptable information or evidence of adequate immunity should be offered immunization at the earliest opportunity, as indicated below. Records of all procedures should be kept by both employer and employee and a system of recall for any necessary boosters should be instituted.

Risk of infection varies with the worker's occupation and the type of facility; immunization policies should allow for these differences.

Vaccines Recommended for All Health Workers

Diphtheria and Tetanus Toxoid

Immunization against diphtheria and tetanus is recommended for all adults in Canada. The opportunity should be taken on entry into health care employment to ensure that the appropriate primary courses and booster doses as described elsewhere in this Guide have been given. Booster doses of Td should be given routinely every 10 years.

Polio Vaccine

Primary immunization with inactivated poliomyelitis vaccine (IPV) is indicated for all health care workers who have not had a primary course of oral poliovirus vaccine (OPV) or IPV. (OPV is not recommended for health care workers because they may shed the virus and inadvertently expose immunocompromised patients to live virus). Persons who have previously been given less than a full primary course of OPV or IPV should have the series completed with IPV regardless of the interval since the last dose.

Rubella Vaccine

All female employees who may become pregnant should be immune to rubella. In addition, all employees of either sex who may have face-to-face contact with pregnant patients should be immune to rubella to avoid transmission of infection to such patients. The immune status of new employees should be determined by review of immunization records or by serological testing. Those who are found to be susceptible should be given rubella vaccine unless it is contraindicated. Adult females should be advised to avoid pregnancy for 3 months after vaccination.

Measles Vaccine

Measles vaccine should be given to health care workers who were born after 1956 and have no documented history of measles or of vaccination with live measles vaccine. Persons born before 1957 have probably been infected naturally and may be considered to be immune. It is not necessary to initiate a serological testing program to detect susceptibles.

Vaccines Recommended for Selective Use

Hepatitis B Vaccine

Hepatitis B vaccine is recommended only for those health care workers repeatedly exposed to blood or blood products. The general categories at high risk are given in the section on Hepatitis B Vaccine (see page 37) but the risk of exposure will differ between settings. Each institution or organization should review its own experience with hepatitis B and develop its own priorities for immunization.

BCG Vaccine

The use of BCG should be limited to health workers who have a negative tuberculin test and a) are at considerable risk of exposure to patients with unrecognized infectious tuberculosis, or b) who handle tubercle bacilli or potentially infectious specimens in a laboratory.

Typhoid Vaccine

Routine immunization of health workers with typhoid vaccine is not recommended. Typhoid vaccination may be considered for laboratory staff who handle cultures of *S. typhi*. After primary immunization, such workers should receive booster doses every 3 years if risk of exposure continues. If more than 3 years have elapsed since the last dose, a single booster dose is sufficient; the primary series need never be repeated.

Typhoid vaccination is not a substitute for proper patient isolation, handwashing, and laboratory technique.

Other Vaccines

Indications for the use of licensed vaccines against cholera, influenza, meningococcal infections, mumps, pertussis, pneumococcal disease, rabies, and yellow fever, are generally the same for health care workers as for the general population. Such vaccines may, however, also be indicated for certain workers believed to be at particularly high risk of exposure (e.g. laboratory workers in specialized reference or research facilities).

Smallpox vaccination is no longer recommended.

Immune Globulins for Specific Risk Situations

Hepatitis A

Prevention of hepatitis A transmission within a hospital should be based on the use of good hygienic practices and patient care techniques, especially proper handwashing and management of potentially infected materials.

Because the risk of hepatitis A transmission in hospital is small, pre-exposure or post-exposure prophylaxis with immune globulin (IG) is not recommended for hospital personnel following routine contact with infected patients. However, personnel who have unusually close contact,

such as direct oral exposure to patients' secretions or excretions soon after onset of illness, should be given IG.

Hepatitis B

Hospital staff or other persons who suffer percutaneous ("needle stick") or mucous membrane exposure to blood or similar products known to contain hepatitis B surface antigen (HBsAg) should be given hepatitis B immune globulin (HBIG) in a dose of 0.06 mL/kg as soon as possible, followed by a second dose one month later. If it is uncertain, but likely, that the blood contained HBsAg, the procedure recommended in the section on Hepatitis B Immune Globulin should be followed.

Part 6

Immunization in Relation to Foreign Travel

A detailed discussion of immunization and other preventive measures required for travellers to other countries is beyond the scope of this booklet. Readers are referred to booklets such as "Don't Drink the Water" or "Things Your Travel Agent Never Told You" (Canadian Public Health Association), "Health Information for International Travel" (U.S. Centers for Disease Control), "Vaccination Certificate Requirements for International Travel and Health Advice to Travellers" (World Health Organization), "Staying Healthy in Warm Climates" and "Immunization — A Guide for International Travellers" (Health and Welfare Canada).

A. Vaccinations Required as a Condition of Entry

Yellow fever vaccination may be required of all persons entering certain countries. It is, moreover, recommended for all travellers to endemic areas whether required or not. The period of validity of the International Vaccination Certificate for yellow fever is 10 years, beginning 10 days after primary vaccination and immediately after re-vaccination. Requirements vary considerably from time to time as changes occur in the geographic distribution of the disease and the effectiveness of eradication programs. Current requirements should be confirmed with local health departments or with the Medical Services Branch, Health and Welfare Canada.

Cholera vaccination is required by relatively few countries. The vaccine provides no protection to the community, but some to the vaccinee. For those countries which require cholera vaccination, the certificate is valid for a period of 6 months commencing 6 days after the first injection or immediately after revaccination.

B. Other Vaccinations

Tourists are generally at lower risk of infection than those persons who intend to live and work in foreign countries. Nevertheless all persons travelling overseas are advised to

ensure that their own routine immunizations, including polio and measles, are up to date. Persons planning to travel off usual tourist routes or work overseas may need to take special precautions such as receiving typhoid vaccine and/or immune globulin for hepatitis A prophylaxis. In specific circumstances, BCG, plague, rabies, or meningococcal vaccines may be useful. They should be administered only in consultation with health officials or on the recommendation of medical authorities in the countries to be visited.

Not all the immunizing agents listed below are required by all travellers. The agents recommended will vary according to the nature of travel, whether staying in urban hotels or in small villages, and the legal requirements for entry into countries being visited. Current information on immunizations required and recommended should be obtained from official health agencies. For details about each agent, the section on individual immunizing agents should be consulted.

The scheduling of immunization is frequently dictated by the traveller, who often waits until the last minute prior to travel, rather than by optimal immunization schedules. Persons who have previously received primary immunization for a disease may require a booster dose of vaccine. Vaccines can usually be administered simultaneously, although those commonly associated with significant local or systemic side effects such as typhoid, plague, and cholera vaccines should be given at different times if possible. Immune globulin should be given just prior to departure where possible but where a live virus vaccine is being given, IG should be administered at least 2 weeks after the vaccine.

International Quarantinable Diseases

1. **Yellow Fever Vaccine:** one dose is required every 10 years.
2. **Cholera Vaccine:** one dose within 6 months of travel complies with the requirements of certain countries. It is not a requirement of the World Health Organization.

Other Immunizing Agents

The immunization status of each traveller should be reviewed in relation to the proposed journey. Among immunizing agents to be considered are:

1. Poliomyelitis vaccine: if the traveller has been previously immunized, one dose of OPV or IPV may be given. For partially immunized or unimmunized persons, see Poliomyelitis Vaccine section.

2. Measles vaccine: a single dose is recommended for all persons aged one year or more who were born after 1956 unless there is a physician-diagnosed history of measles or a documentation of immunization with live measles vaccine.

3. Tetanus and Diphtheria Toxoids: boosters are recommended every 10 years. See specific sections for details.

4. Typhoid vaccine: for travel to countries where typhoid fever is common and hygiene questionable. Unimmunized persons need a primary series; otherwise a booster is given every 3 years.

5. Meningococcal vaccine: one dose of a polyvalent vaccine for travel to areas experiencing epidemics.

6. Plague vaccine: for indications see page 56. For the unimmunized, a primary series is 3 doses, 2 given 4 weeks apart and a 3rd 3 to 6 months later; boosters are needed every 1 to 2 years.

7. Hepatitis B vaccine: travellers who plan to undertake medical work in areas with a high prevalence of hepatitis B for prolonged periods should be considered at risk and receive hepatitis B vaccine if previously unimmunized or known to be susceptible.

8. Immune Globulin (IG): for prophylaxis against hepatitis A infection, IG may be given according to the following table. A test for hepatitis A IgG antibody will indicate whether IG is necessary for those working in or travelling frequently to endemic areas. IG should be given every 4 to 6 months in the doses shown in the lower half of the table to persons continuing to reside abroad in tropical or developing countries.

Length of Stay	Body Weight (kg)	Dose (mL)
Under 3 months	<23	0.5
	23-45	1.0
	>45	2.0
Over 3 months	<23	1.0
	23-45	2.5
	>45	5.0

9. Rabies vaccine: pre-exposure immunization should be considered for persons intending to live or work in highly endemic areas especially where rabies control programs for domestic animals are inadequate.

C. Immunization Schedule

Only agents required for the proposed journey should be given. Few persons will require all of the immunizations. Adjustments in dates of immunization may be necessary because of administrative and/or other reasons.

5-Week Course	Week					
Vaccine	0	1	2	3	4	5
Typhoid	X				X	
Polio	X					
Measles	X					
Cholera						X*
Diphtheria/Tetanus		X				
Yellow Fever	X					
IG						X
Plague		X				X

* A second dose is not generally needed to meet international requirements; if given it should be 4 weeks after the first.

If time does not permit completion of the course as presented, the second doses of cholera, typhoid and plague vaccines can be given as close together as one week although the degree of protection may not be the same as in the optimally spaced schedule. IG should always be administered at least 2 weeks after live virus vaccines and as close to the time of departure as possible.

D. Malaria prophylaxis

Travellers should be advised regarding chemoprophylaxis against malaria as no licensed vaccine is available. Current information concerning malaria risk and areas with chloroquine-resistant strains as well as recommended drugs for prophylaxis is available from local health departments or Medical Services Branch, Health and Welfare Canada.

Appendix

Licensed Immunizing Agents Against Microbial Disease

The following list of immunizing agents and the manufacturers licensed to manufacture and/or market them in Canada reflects the situation in December 1983. However, not all licensed products of all manufacturers will necessarily be available in all parts of Canada at all times. The demand for some vaccines is often regional and seasonal or cyclical and, because immunizing agents lose potency over time, large stocks are unlikely to be kept except where a steady demand can be anticipated.

The formulation of certain preparations, notably influenza vaccine, will vary from time to time depending, for instance, on the strains of virus expected to be a major cause of illness. Provincial Departments of Health sometimes contract for a large supply of the appropriate formulation from a particular source, and can generally advise on the availability of recommended vaccines.

The product names used in the list are in common use and are not necessarily those under which the license for the product was issued.

Active Immunizing Agents

Antigen	Company	Description or Comments
<i>B.C.G. Vaccine</i>	Connaught Institut Armand-Frappier	Intracutaneous (live) Intracutaneous (live) Percutaneous (live)
<i>Cholera Vaccine</i>	Connaught	
<i>Diphtheria Toxoid</i>	Connaught Institut Armand-Frappier	Fluid D50 Lf/mL Fluid D4 Lf/mL, for immunization of reactors Fluid D50 Lf/mL

Antigen	Company	Description or Comments
<i>Diphtheria and Tetanus (DT and Td)</i>	Connaught	Fluid D50 T10/mL (DT) Fluid D10 T10/mL* Adsorbed D25 T5/0.5 mL (DT) Adsorbed d2 T5/0.5 mL* (Td)
	Institut Armand-Frappier Wyeth	Fluid D40 T10/mL (DT) Fluid D10 T10/mL* Adsorbed D10 T5/0.5 mL (DT) Adsorbed d1.4 T5/0.5 mL* (Td)
<i>Diphtheria, Pertussis and Tetanus (DPT)</i>	Connaught	Fluid D40 T8/mL Adsorbed D25 T5/0.5 mL
	Institut Armand-Frappier Wyeth	Fluid D30 T10/mL Adsorbed d7.5 T5/0.5 mL
<i>Diphtheria, Tetanus and Polio (Td-Polio and DT-Polio)</i>	Connaught	Fluid D10 T10/mL* Adsorbed D25 T5/0.5 mL (DT) and d2 T5/0.5 mL* (Td)
<i>Diphtheria, Pertussis, Tetanus and Polio (DPT-Polio)</i>	Connaught	Fluid D40 T8/mL Adsorbed D25 T5/0.5 mL
<i>Hepatitis B Vaccine</i>	Merck, Sharp & Dohme	Subunit, Adsorbed
<i>Influenza Vaccine</i>	Connaught	Whole virus
	Institut Armand-Frappier	Split virus
	Merck, Sharp & Dohme	Whole virus
	Parke-Davis	Split virus
<i>Measles Vaccine</i>	Connaught	Live, Attenuated
	Merck, Sharp & Dohme	Live, Attenuated

* A dilute strength for adults and recall doses.

Antigen	Company	Description or Comments
<i>Measles and Rubella Vaccine</i>	Merck, Sharp & Dohme	Live, Attenuated
<i>Measles, Mumps and Rubella Vaccine</i>	Merck, Sharp & Dohme	Live, Attenuated
<i>Meningococcal Polysaccharide Vaccine</i>	Merck, Sharp & Dohme Connaught	Group C Groups A and C Groups A, C, Y and W-135
<i>Mumps Vaccine</i>	Merck Sharp & Dohme	Live, Attenuated
<i>Pertussis Vaccine</i>	Connaught	
<i>Plague Vaccine</i>	Cutter	
<i>Pneumococcal Vaccine</i>	Merck, Sharp & Dohme	Polyvalent: 23 capsular types
<i>Poliovirus Vaccine</i>	Connaught Institut Armand-Frappier	Live, Oral (Sabin) Trivalent
<i>Poliomyelitis Vaccine, Inactivated</i>	Connaught	Inactivated (Salk) Trivalent
<i>Rabies Vaccine</i>	Connaught Connaught Mérieux Wyeth	Semple type Hamster Kidney for pre-exposure only Human Diploid Cell Human Diploid Cell, Subvirion
<i>Rubella Vaccine</i>	Connaught Merck, Sharp & Dohme	Live, Attenuated Live, Attenuated
<i>Rubella and Mumps Vaccine</i>	Merck, Sharp & Dohme	Live, Attenuated

Antigen	Company	Description or Comments
<i>Smallpox Vaccine</i>	Connaught	live; restricted availability
<i>Staphylococcus Toxoid</i>	Connaught	
<i>Tetanus Toxoid</i>	Connaught	Fluid T10/mL
		Adsorbed T5/0.5 mL
	Institut Armand-Frappier	Fluid T10/mL
	Lederle	Adsorbed T5/0.5 mL
	Wyeth	Adsorbed T5/0.5 mL
<i>Tetanus and Polio</i>	Connaught	Fluid T10/mL Adsorbed T5/0.5 mL
<i>Typhoid Vaccine</i>	Connaught	Heat killed, phenol preserved
<i>Yellow Fever Vaccine</i>	Connaught	Live, Attenuated

Passive Immunizing Agents

Product	Company	Description or Comments
<i>Botulism Antitoxin (Equine)</i>	Connaught	Trivalent, Types A, B and E
	Connaught	Type E
<i>Diphtheria Antitoxin (Equine)</i>	Connaught	
<i>Gas Gangrene Antitoxin (Equine)</i>	Connaught	<i>C. perfringens</i> , <i>C. septicum</i> and <i>C. oedematiens</i>
<i>Globulin Immune (Human)</i>	Armour	
	Connaught	
	Cutter	
	Hyland	
	Osterreichisches Institut Fur Haemoderivate	
<i>Globulin Immune, Intravenous (Human)</i>	Cutter Sandoz	
<i>Hepatitis B Immune Globulin (Human)</i>	Connaught	
	Cutter	
<i>Pertussis Immune Globulin (Human)</i>	Cutter	
	Hyland	
	Osterreichisches Institut Fur	
	Haemoderivate	
<i>Rabies Immune Globulin (Human)</i>	Connaught	
	Cutter	
	Mérieux	
<i>Tetanus Immune Globulin (Human)</i>	Armour	
	Connaught	
	Cutter	
	Hyland	
	Osterreichisches Institut Fur	
	Haemoderivate	

Product	Company	Description or Comments
<i>Varicella-Zoster Immune Globulin</i>	Massachusetts Public Health Biologic Laboratories	Human Origin

Note:

The names of drugs in the text are commonly used and may not necessarily be identical with names used in pharmacopoeal compendia. Newly developed and presently unlicensed active or passive immunizing agents may be available for physicians to immunize individuals through Emergency Drug Release procedures as contained in Section C.08.010 of the Food and Drug Regulations.

Upon confirmation that the supply is available, the physician should contact the Bureau of Biologics, Health Protection Branch, Tunney's Pasture, Ottawa, Ontario, K1A 0L2, Telephone (613) 990-8064, 990-8959 or after hours 993-3660, outline the problem, identify the confirmed source of supply and request release of the agent. Where appropriate the Bureau will contact the supplier directly and authorize release.

Licensed Manufacturers

Armour Pharmaceutical Company
USV Canada Inc.
2501 Stanfield Road
Mississauga, Ontario
L4Y 1R9
(416) 276-4711

Connaught Laboratories Ltd.
1755 Steeles Avenue West
Willowdale, Ontario
M2N 5T8
(416) 667-2701

Cutter Laboratories Ltd.
8241 — 30th Street S.E.
Calgary, Alberta
T2C 1H7
(403) 279-7735

Hyland Division Travenol Labs. Inc.
Travenol Laboratories Inc.
6405 Northam Drive
Malton, Ontario
(416) 677-6730

Institut Armand-Frappier
531 Boulevard des Prairies
Case Postale 100
Laval-des-Rapides, Québec
H7N 4Z3
(514) 687-5010

Institut Mérieux
Rhône-Poulenc Pharma Inc.
8580 Esplanade Avenue
Montreal, Québec
H2P 2R9
(514) 384-8220

Licensed Manufacturers

Lederle Laboratories
635 Dorchester Boulevard W.
Montreal, Québec
H3B 4A6
(514) 866-5611

Massachusetts Public Health Biologic Laboratories
Canadian Red Cross Society
Blood Transfusion Service
95 Wellesley Street East
Toronto, Ontario
M4Y 1H6
(416) 596-3240

Merck, Sharp and Dohme
P.O. Box 1005
Pointe Claire-Dorval, Québec
H9R 4P8
(514) 695-7550

Osterreichisches Institut Fur Haemoderivate

Parke Davis and Company
Box 633 Station A
Scarborough, Ontario
M1K 5C5
(416) 228-2200

Sandoz Pharmaceuticals
109 Consumers Drive
Whitby, Ontario
L1N 1C4
(416) 668-5332

Wyeth Laboratories Inc.
P.O. Box 370
Downsview, Ontario
M3M 3A8
(416) 630-0280